Exhibit 23

UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF NEW YORK

IN RE: ACETAMINOPHEN – ASD-ADHD PRODUCTS LIABILITY LITIGATION	) MDL No. 3043) Case No. 1:22-md-03043-DLC
THIS DOCUMENT RELATES TO: All Cases, 1:22-md-03043	) JUDGE DENISE COTE

WEDNESDAY, AUGUST 9, 2023

CONFIDENTIAL - PURSUANT TO PROTECTIVE ORDER

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Videotaped deposition of Eric Hollander, M.D. DFAPA, FACNP, held at the Lanier Law Firm, 126 East 56th Street, New York, New York, commencing at 9:43 a.m. Eastern, on the above date, before Carrie A. Campbell, Registered Diplomate Reporter, Certified Realtime Reporter, Illinois, California & Texas Certified Shorthand Reporter, Missouri, Kansas, Louisiana & New Jersey Certified Court Reporter.

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GOLKOW LITIGATION SERVICES
877.370.DEPS
deps@golkow.com

A P P E A R A N C E S:

DOVEL & LUNER
BY: GREG DOVEL
greg@dovel.com
JULIEN ADAMS (VIA ZOOM)
julien@dovel.com
201 Santa Monica Boulevard, Suite 600
Santa Monica, California 90401
(310) 656-7066

and

TRACEY & FOX
BY: SEAN P. TRACEY (VIA ZOOM)
stracey@traceylawfirm.com
LAWRENCE TRACEY (VIA ZOOM)
ltracey@traceylawfirm.com
440 Louisiana Street, Suite 1901
Houston, Texas 77002
(713) 495-2333

and

THE LANIER LAW FIRM, PLLC
BY: EVAN M. JANUSH (VIA ZOOM)
evan.janush@lanierlawfirm.com
CATHERINE HEACOX
catherine.heacox@lanierlawfirm.com
LEILA AYACHI (VIA ZOOM)
leila.ayachi@lanierlawfirm.com
126 East 56th Street, 6th Floor
New York, New York 11758
(212) 421-2800

and

HOLWELL SHUSTER & GOLDBERG LLP
BY: DANIEL M. SULLIVAN (VIA ZOOM)
dsullivan@hsgllp.com
425 Lexington Avenue
New York, New York 10017
(646) 837-5151

and

KELLER POSTMAN LLC
BY: LAUREN SCHULTZ
lauren.schultz@kellerpostman.com
REBECCA KING (VIA ZOOM)
rebecca.king@kellerpostman.com
ASHLEY C. KELLER (VIA ZOOM)
ashley.keller@kellerpostman.com
ASHLEY BARRIERE (VIA ZOOM)
ashley.barriere@kellerpostman.com
ROSIE ROMANO (VIA ZOOM)
rosie.romano@kellerpostman.com
J.J. SNIDOW (VIA ZOOM)
jj.snidow@kellerpostman.com
150 North Riverside Plaza, Suite 4100
Chicago, Illinois 60606
(312) 741-5220

and

WATTS GUERRA LLC
BY: MIKAL C. WATTS
mcwatts@wattsguerra.com
HAILEY WATTS
hwatts@wattsguerra.com
RUSS ABNEY (VIA ZOOM)
rabney@wattsguerra.com
SHELLY SANFORD (VIA ZOOM)
ssanford@wattsguerra.com
Millennium Park Plaza RFO
Suite 410, C112
Guaynabo, Puerto Rico 00966
(210) 447-0500

and

WAGSTAFF & CARTMELL
BY: DARYL DOUGLAS (VIA ZOOM)
ddouglas@wcllp.com
4740 Grand Avenue, Suite 300
Kansas City, Missouri 64112
(816) 701-1100

and

THE CARLSON LAW FIRM
BY: EMILY MARLOWE
emarlowe@carlsonattorneys.com
1717 North Interstate Highway 35,
Suite 305
Round Rock, Texas 78664
(512) 671-7277

and

BEASLEY, ALLEN, CROW, METHVIN,
PORTIS & MILES
BY: W. ROGER SMITH, III (VIA ZOOM)
roger.smith@beasleyallen.com
218 Commerce Street
Montgomery, Alabama 36104
(800) 898-2034
Counsel for Plaintiffs

BARNES & THORNBURG LLP
BY: JAMES F. MURDICA
jmurdica@btlaw.com
SARAH E. JOHNSTON
sjohnston@btlaw.com
MITCHELL CHARCHALIS
mcharchalis@btlaw.com
2029 Century Park East, Suite 300
Los Angeles, California 90067-2904
(310) 284-3880

and

BARNES & THORNBURG, LLP
BY: KARA KAPKE (VIA ZOOM)
kara.kapke@btlaw.com
11 South Meridian Street
Indianapolis, Indiana 46204
(317) 236-1313

and

BARNES & THORNBURG LLP
BY: DEANNA LEE (VIA ZOOM)
dlee@btlaw.com
555 12th Street N.W., Suite 1200
Washington, DC 20004-1275
(202) 289-1313

and

BARNES & THORNBURG LLP
BY: JESSICA BRENNAN (VIA ZOOM)
jessica.brennan@btlaw.com
67 East Park Place, Suite 500
Morristown, New Jersey 07960
(973) 775-6101
Counsel for Johnson & Johnson
Consumer, Inc.

BARNES & THORNBURG LLP
BY: NADINE KOHANE (VIA ZOOM)
nkohane@btlaw.com
390 Madison Avenue, 12th Floor
New York, New York 10017
(646) 746-2000
Counsel for CVS Pharmacy, Inc., CVS
Health Corporation, Walgreen Co.,
Walgreens Co., and Walgreens Boots
Alliance, Inc.

Page 6

BARNES & THORNBURG LLP
BY: SANDRA M. KO (VIA ZOOM)
sko@btlaw.com
555 12th Street N.W., Suite 1200
Washington, DC 20004-1275
(202) 289-1313
Counsel for Costco Wholesale Corporation

ARNOLD & PORTER, LLP
BY: RAYNE ELLIS (VIA ZOOM)
rayne.ellis@arnoldporter.com
250 West 55th Street
New York, New York 10019
(212) 836-8000
Counsel for Dollar Tree Inc., 7-Eleven, and Family Dollar, Inc.

KING & SPALDING LLP
BY: LUKE BOSSO (VIA ZOOM)
lbosso@kslaw.com
1700 Pennsylvania Avenue NW
Washington, DC 20006
(202) 737-0500
Counsel for Walmart Inc., and Wal-Mart Stores, Inc.

MORRISON & FOERSTER LLP
BY: LYNDSEY CAIN (VIA ZOOM)
lcain@mofo.com
250 West 55th Street
New York, New York 10019-9601
(212) 468-8000
Counsel for Target Corporation

Page 7

DUANE MORRIS LLP
BY: SEAN K. BURKE (VIA ZOOM)
sburke@duanemorris.com
901 New York Avenue N.W., Suite 700 East
Washington, DC 20001-4795
(202) 776-5236
Counsel for Dollar General, Dollar General Corporation

SMITH SOVIK KENDRICK & SUGNET
BY: DAVID M. KATZ (VIA ZOOM)
dkatz@smithsovik.com
250 South Clinton Street, Suite 600
Syracuse, New York 13202
(315) 474-2911
Counsel for Rite Aid

STONE DEAN LLP
BY: JOSEPH A. LARA (VIA ZOOM)
jlara@stonedeanlaw.com
21052 Oxnard Street
Woodland Hills, California 91367
(818) 999-2232
Counsel for The Kroger Co.

HAIGHT BROWN & BONESTEEL LLP
BY: KATIE M. TRINH (VIA ZOOM)
ktrinh@hbblaw.com
555 South Flower Street, 55th Floor
Los Angeles, California 90071
(213) 542-8000
Counsel for Big Lots Stores-PNS, LLC

ALSO PRESENT:
JACKIE KOSTICK, King & Spalding
LAURA SHANNON, summer associate, Keller Postman LLC

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VIDEOGRAPHER:
DANNY ORTEGA
Golkow Litigation Services

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VIDEOGRAPHER: We are now on the record. My name is Danny Ortega, and I'm the legal videographer for Golkow Litigation Services.

Today's date is August 9, 2023, and the time is 9:43 a.m.

This video deposition is being held at 126 East 56th Street, New York, New York, in the matter of Acetaminophen (Tylenol) ASD-ADHD Products Liability Litigation.

The deponent today is Eric Hollander.

All counsel will be noted on the stenographic record.

The court reporter today is Carrie Campbell and will now swear in the witness.

ERIC HOLLANDER, M.D. DFAPA, FACNP, of lawful age, having been first duly sworn to tell the truth, the whole truth and nothing but the truth, deposes and says on behalf of the Defendant Johnson & Johnson, as follows:

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DIRECT EXAMINATION

QUESTIONS BY MR. MURDICA:

Q. Good morning, Dr. Hollander.

A. Good morning.

Q. My name is Jim Murdica. I'll be examining you today.

Do you know Dr. Robert Cabrera?

A. Yes, I do.

Q. Okay. And when did you first met Dr. Robert Cabrera?

A. In preparing for my expert report, I had an opportunity to speak with him.

Q. Now, that was in 2023?

A. That's correct.

Q. And you reference him several times in your report and rebuttal report as somebody that you're relying on as a basis for your opinions, correct?

A. That's correct.

Q. Okay. Did you have the opportunity to review my examination of Dr. Cabrera?

A. No.

Q. Have you been provided my

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examination of Dr. Cabrera?

A. Yes.

Q. Okay. When were you provided that?

A. Prior to this deposition.

Q. And when? Today? A week ago? Two days ago?

A. Sometime between, I believe, when I filed my rebuttal and when we're meeting today.

Q. Okay. And if I understood you, you chose not to review it; is that right?

A. I didn't review it. I didn't have time to review it.

Q. Okay. Did you skim it?

A. No.

Q. Did you open it at all?

A. No.

Q. Okay. Is there any opinion -- well, let me lay some foundation here.

You offered a rebuttal report in this litigation, right?

A. That's correct.

Q. And an initial report?

A. Yes.

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Q. And an amended -- well, an initial report and an amended report and a rebuttal report, right?
A. Right. And an amended causation report and a rebuttal report.
Q. Okay. And is there anything as a result of Dr. Cabrera's testimony here that you want to change in your three reports that you've issued?
A. No.
Q. So you, sitting here today, have no idea what happened or didn't happen or said or was said at Dr. Cabrera's deposition; is that fair?
A. I think it's fair. I haven't reviewed the deposition.
Q. Okay. Your counsel handed me a paper before we started today.
Did you see him do that?
A. Yes, I did.
Q. Okay. And is this something that you reviewed?
A. Yes.
(Hollander Exhibit 50 marked for identification.)

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QUESTIONS BY MR. MURDICA:
Q. Okay. I'm going to mark it for the sake of the record as Exhibit 51. 50.
Do you recognize this, Dr. Hollander, as what was handed to me before we started?
A. Yes, I recognize it.
Q. Okay. Are you relying on Exhibit 50 for -- to support your causation opinions here?
MR. DOVEL: Objection. Form.
QUESTIONS BY MR. MURDICA:
Q. Dr. Hollander, I'll ask a new question.
Are you relying on Exhibit 50 for any opinion you have here?
MR. DOVEL: Objection. Form.
THE WITNESS: I'm incorporating this material, along with all of the other material that I have from my materials considered, and it is consistent with my opinion.
QUESTIONS BY MR. MURDICA:
Q. Okay. Dr. Hollander, do you know that Dr. Cabrera said that there's not

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enough there in that paper on the Notch or SOX pathway to influence his causation opinion?
MR. DOVEL: Objection. Form.
THE WITNESS: I'm not aware of whether or not he made that statement.
QUESTIONS BY MR. MURDICA:
Q. Okay. Dr. Cabrera -- I mean, sorry, Dr. Hollander, are you, sitting here today, going to tell us that the Notch signaling or SOX pathway is a biologically plausible mechanism that you are going to rely on for your opinions here relating to acetaminophen and the outcomes of ASD and ADHD?
A. Well, it's not a pathway that I considered in my amended expert report or in my rebuttal report, but it's additional information that supports my opinions with regards to exposure and outcome.
Q. Okay. Dr. Hollander, have you ever, in your regular work, researched Notch signaling?
A. No.
Q. Okay. In your regular work,

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have you ever done any research or experimentation regarding the SOX2 pathway?
A. No.
Q. Okay. In your expert report, did you identify the hippocampus as an area of the brain that is related to the underlying development of ASD or ADHD?
A. Well, yes. The hippocampus is a, you know, essential region that's involved in learning and memory that plays a critical role across neurodevelopmental disorders, and that can be disrupted by exposure that affects neurodevelopment.
Q. Okay. The study that you have in front of you, Exhibit 50, doesn't say anything about ASD or ADHD, correct?
A. No, I don't see the words "ASD" or "ADHD" in the abstract.
Q. And it's a study of mice, correct?
A. That's correct.
Q. When did you review that, Exhibit 50?
A. Over the weekend.
Q. Okay. And if Dr. Cabrera is

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not relying on that for his opinion, that doesn't change what you're doing with respect to it, correct?

MR. DOVEL: Objection. Form.

THE WITNESS: Whether or not he relies on this specific article for his opinion, what I said before holds true, that it's a piece of evidence that I've reviewed that is supportive of my opinions.

QUESTIONS BY MR. MURDICA:

Q. Okay. In your -- so, Dr. Hollander, your regular job is counseling patients who have primarily OCD and autism, correct?

MR. DOVEL: Objection. Form.

THE WITNESS: Well, I'm not sure what you mean by "regular job," but, you know, among my different roles, one of my activities is, yes, I'm involved in clinical care of patients with ASD and ADHD and OCD and other neurodevelopmental and psychiatric disorders.

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QUESTIONS BY MR. MURDICA:

Q. Yeah.

Dr. Hollander, what I meant is, your regular day-to-day job does not normally entail testifying for plaintiffs' lawyers in depositions, right?

A. I have been involved in testifying for plaintiffs' lawyers as part of the various roles that I've been involved in. I wouldn't say I do that on a day-to-day basis, but that is an activity that I have done as part of my overall activities.

MR. MURDICA: I guess we have a tech issue.

Do I understand that correctly?

MS. JOHNSTON: Let's off the record for a sec.

VIDEOGRAPHER: Yeah, the time is 9:51 a.m. We are off the record.

(Off the record at 9:51 a.m.)

VIDEOGRAPHER: The time right now is 9:56 a.m. We are back on the record.

QUESTIONS BY MR. MURDICA:

Q. Dr. Hollander, there was a technical issue.

Are you ready to proceed?

A. Yes, I am.

Q. Okay. When we stopped for the technical issue, I was asking about your testimony here versus your regular day-to-day job.

Do you remember that question?

A. Yes, I do.

Q. Okay. And you testified that you have in the past testified for plaintiffs' lawyers, correct?

A. That is correct.

Q. Right.

And you offered opinions while being paid for plaintiffs' lawyers in the Mirapex litigation; is that right?

A. Well, that's correct. I offered opinions in the Mirapex litigation, and I was compensated for my time.

Q. You offered opinions while being paid by plaintiffs' lawyers in the Abilify litigation; is that correct?

A. That's correct. I offered opinions in the Abilify litigation as well

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and was compensated for my time.

Q. Okay. Have you taken money from the plaintiffs' Bar to offer testimony in any other cases between Abilify and this one?

MR. DOVEL: Objection. Form.

THE WITNESS: I don't believe so.

QUESTIONS BY MR. MURDICA:

Q. Okay. Do you disclose to your patients that you've taken money from the plaintiffs' Bar?

MR. DOVEL: Objection. Form.

THE WITNESS: Well, I don't believe that I have a discussion with each of my patients if -- if the interactions that I'm having with my patients have any relevance to the testimony, for example, that I've offered. So, no.

QUESTIONS BY MR. MURDICA:

Q. Okay. Dr. Hollander, you've published papers before, right?

A. Yes, I have.

Q. In the disclosure section, do

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you include that you've taken hundreds of thousands of dollars from the plaintiffs' Bar?

MR. DOVEL: Objection. Form.

THE WITNESS: In articles that I publish, I disclose if there are relevant conflicts of interest.

QUESTIONS BY MR. MURDICA:

Q. Okay. So the answer to my question is, to date, you haven't disclosed in any article that you've published that you've taken hundreds of thousands of dollars from the plaintiffs' Bar in the United States, correct?

MR. DOVEL: Objection. Form.

THE WITNESS: I don't believe that there has been an occasion where I've published material where that would be a relevant conflict of interest to disclose.

QUESTIONS BY MR. MURDICA:

Q. And, therefore, you haven't done it to date, correct?

A. Well, if I -- if I were to publish and it was relevant to compensation

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that I've received -- and this would be the case whether it was compensation related to, you know, research grants or consulting activities or speaking or testimony -- then I would disclose the relevant conflict.

Q. Okay. And, Dr. Hollander, have you ever disclosed as a relevant conflict money you've taken from the plaintiffs' Bar?

A. I don't believe that I've published any material that would be relevant to the issues, for example, that I've offered opinion on and, therefore, I wouldn't be bound to disclose because it wouldn't have been a conflict of interest.

Q. And therefore, Dr. Hollander, your testimony is you haven't done it because it hasn't been necessary, in your opinion, correct?

MR. DOVEL: Objection. Form.

THE WITNESS: Well, that -- that's correct. I don't believe that I've --

QUESTIONS BY MR. MURDICA:

Q. Okay.

A. -- published anything where it

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would require a disclosion {sic} related to that because I don't believe that I've published anything that would be related to material that I testified on.

Q. You maintain a website called Spectrum Neurosciences, correct?

A. That's one of the websites that I maintain, correct.

Q. Do you have a disclosure on there about the money that you've taken from the plaintiffs' Bar?

MR. DOVEL: Objection. Form.

THE WITNESS: I don't believe that there is anything on that website that relates to any material, actually, that would relate to testimony in any products liability case, no.

QUESTIONS BY MR. MURDICA:

Q. Dr. Hollander, have you ever published anything on acetaminophen?

A. I don't believe that I've published anything on acetaminophen.

Q. Dr. Hollander, have you ever conducted any research regarding

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acetaminophen prior to your engagement in this litigation?

A. I don't believe that I've been involved in prior research with acetaminophen.

Q. Have you conducted any animal studies with respect to acetaminophen?

A. No.

Q. Have you ever conducted animal studies at all, Dr. Hollander?

A. Yes.

Q. Okay. And was it you conducting them or supervising them?

A. Both.

Q. Okay. And is that something you still do?

A. Well, I would say that I work closely with animal researchers as it relates to translational research that I do. So -- and if that's the case, then I would be working with preclinical investigators to inform the work that I do in terms of clinical investigations. That's the point of translational research, to translate findings from animal models into human studies.

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Q. So if you wanted to conduct animal research on acetaminophen, you could, right?
A. I don't -- well, if I -- if I wanted to conduct animal research with acetaminophen, I wouldn't do that myself, so I would probably partner with a preclinical investigator.
Q. Okay. And to date, you haven't done that, right, Dr. Hollander?
A. That's correct.
Q. Okay. And if I asked you the same questions about human research or study -- human study, you haven't done that with respect to acetaminophen either, correct?
MR. DOVEL: Objection. Form.
THE WITNESS: Well, that's correct. I haven't conducted clinical investigations regarding acetaminophen either.
QUESTIONS BY MR. MURDICA:
Q. Okay. If we looked at your profile on Spectrum Neurosciences, would we see anything at all about attention-deficit/

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hyperactivity disorder?
A. I believe you would.
Q. Okay. Is that one of your specialties, Doctor?
A. That is one of my specialties.
Q. Okay. If somebody asked -- if your colleagues, would they say attention-deficit/hyperactivity disorder is one of your specialties, Dr. Hollander?
MR. DOVEL: Objection. Form.
THE WITNESS: Yes, I have expertise in all of the neurodevelopmental disorders.
QUESTIONS BY MR. MURDICA:
Q. Okay. Dr. Hollander, is it your opinion today that acetaminophen causes the outcome of autism or ADHD in human beings when used in utero?
MR. DOVEL: Objection. Form.
THE WITNESS: It is my opinion now, today, that acetaminophen exposure in utero or in pregnant women can cause neurodevelopmental disorders, including ASD and ADHD, in offspring, in humans.

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QUESTIONS BY MR. MURDICA:
Q. Okay. And when did Dr. Hollander first come to that opinion?
A. I came to that opinion prior to writing my amended causation expert report.
Q. Okay. And I just want to make sure we understand each other by the way we name the reports.
You issued an initial report in this litigation, right?
A. Correct.
Q. In that initial report, you did not say that acetaminophen causes -- exposure during pregnancy causes autism or ASD in the offspring, correct?
A. In my initial report I offered a number of opinions, but in the initial report I didn't specifically state that acetaminophen causes ASD or ADHD.
Q. And, Doctor, that's because at the time you signed your initial report, that was not one of the opinions you were offering, correct?
A. No.
Q. Okay. So at the time you --

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sorry. At the time you signed your initial report, you were intending to offer the opinion that acetaminophen exposure in pregnancy causes ASD and ADHD in the offspring?
A. No. At the time of my initial report, I held the opinion that acetaminophen causes ASD and ADHD in offspring.
Q. Okay. And is it your testimony that it was in your initial report? That that opinion was in there?
A. No.
Q. Okay.
A. I'm saying that I held that opinion. I'm -- if you like, I can expand on that.
Q. Well, when, Dr. Hollander, did you first come to hold that opinion?
A. Prior to my initial report.
Q. Okay. Was it sometime in 2023?
A. Yes.
Q. Okay. On -- for your Spectrum Neurosciences -- that's a business, right?
A. That's a subspecialty clinical practice that specializes in

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neurodevelopmental disorders.
Q. Okay. And there's three other medical doctors that work with you as part of Spectrum Neurosciences, right?
A. There are several other medical doctors as well as experts in neuropsychology and psychology and people who have expertise in other specialties that provide critical treatment for these individuals. So people who are also ancillary professionals as well.
Q. Do you remember my question?
A. Your question was were there three other doctors who work with me in that clinical practice?
Q. Medical doctors, Dr. Hollander. There's three other medical doctors that work with you?
A. I believe that there's three other medical doctors.
Q. Okay. And, Dr. Hollander, which of those three other medical doctors have you told that you hold the opinion that in utero acetaminophen exposure causes autism and ADHD?
A. I'm not sure that I had

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specific discussions with those three individuals regarding this matter at hand.
Q. Okay. You haven't told them, right?
A. I don't recall whether or not I told them.
Q. Have you told anyone other than the plaintiffs' lawyers?
A. Yes.
Q. Okay. Who have you -- let's go through who you've told.
A. Well, in discussions with patients who have been considering getting pregnant, for example, or who have been pregnant, if the topic was of relevance, I may have had a discussion.
Q. And that was in 2023, right, Dr. Hollander?
A. That's correct.
Q. Okay. Outside of patients that you may or may not have told that you believe that acetaminophen causes autism and ADHD, have you told any medical professionals that you believe that?
A. Well, I have had discussions

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with other individuals who have expertise in the matters at hand, and I've questioned them with regards to their opinion, and I've discussed my thoughts as well.
Q. And some of those people that you've had discussions with are paid by the plaintiffs' lawyers as well, right?
A. Yes. Some of those individuals are experts on behalf of the plaintiffs, yes.
Q. You know that your opinion that you're offering here on causation is not to -- at this point is not widely accepted, correct?
A. No.
MR. DOVEL: Objection. Objection. Form.
QUESTIONS BY MR. MURDICA:
Q. Okay.
A. I don't think I would agree with that statement.
Q. Okay. Dr. Hollander, are you an obstetrician?
A. No, I am not.
Q. Okay. When a woman is pregnant and is asking for advice on medication during

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pregnancy, would the first stop be an obstetrician?
MR. DOVEL: Objection.
QUESTIONS BY MR. MURDICA:
Q. To ask for advice?
MR. DOVEL: Form. Objection. Form.
THE WITNESS: You know, if a woman is pregnant or considering being pregnant, then they might seek information from different sources. So it might be an obstetrician. It might be someone who deals with high-risk pregnancies because these issues may be particularly of interest in people who specialize in high-risk pregnancies. It might be someone who specializes in maternal-fetal medicine. So -- and also someone who has expertise who can discuss the risks and benefits of different kinds of medications for both the mother and for the offspring.
QUESTIONS BY MR. MURDICA:
Q. Okay. Dr. Hollander, are you

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an MFM? Are you an expert in maternal-fetal medicine?

A. Well, I see many women who have issues around medication usage during pregnancy, and I can offer advice.

I also sometimes refer patients to individuals, for example, within my practice or outside of the practice who also have expertise in maternal-fetal medicine.

So I would want to seek and get consultation from individuals with a range of experience and knowledge and background.

Q. Dr. Hollander, are you a member of the Society of Maternal-Fetal Medicine?

A. No.

Q. Okay. Are you a member of the American College of Obstetricians and Gynecologists?

A. No.

Q. Do you recognize ACOG as the body that has expertise in obstetrics and gynecology?

A. Yes.

Q. Everyone that's a member of ACOG is board certified in obstetrics and

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gynecology, correct?

A. I would think so, but I'm not certain about that.

Q. Okay. Have you seen what the American College of Obstetricians and Gynecologists have said about the relationship between acetaminophen and the outcomes of autism and ADHD?

A. I have had the opportunity to review different consensus statements issued by different bodies that relate to this matter.

Q. Right.

A. And I'm aware that there's different consensus statements and opinions that have been offered on this matter.

Q. The 60,000 board certified obstetricians and gynecologists in the United States disagree with your opinions here, and you know that, right?

MR. DOVEL: Objection. Form.

THE WITNESS: Well, again, I would say that there are different bodies that have offered different opinions with regards to this matter.

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QUESTIONS BY MR. MURDICA:

Q. Does ACOG agree with you, Dr. Hollander?

MR. DOVEL: Objection. Form.

THE WITNESS: Not at this time.

QUESTIONS BY MR. MURDICA:

Q. Okay. And that was my original question, Dr. Hollander.

A. Yes.

Q. At this time --

A. Right.

Q. -- your opinion that acetaminophen causes ASD and ADHD during pregnancy is controversial, correct?

MR. DOVEL: Objection. Form.

THE WITNESS: Well, I would say that there are different opinions, and I do think that that is consistent with the history of medicine.

As, you know, additional evidence appears and as different analyses appear in the literature, that influences recommendations and treatment practice. And those recommendations evolve over time, yes.

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QUESTIONS BY MR. MURDICA:

Q. Right.

For example, back in the early 2000s, you were offering opinions regarding the MMR and thimerosal issues, correct?

A. No.

Q. Okay. I didn't mean offering opinions for plaintiffs' lawyers. I meant you were tracking that and talking about it in your regular work, correct?

A. No. I was not offering opinions with regards to that matter.

Q. Okay. You know that initially vaccines were thought to be related to the outcome of autism, right?

A. I understand that that's an area of controversy. It's not something -- that's not an opinion that I've held.

Q. Okay. Well, let's ask you today, Dr. Hollander.

Does the MMR vaccine cause autism?

A. As of today, no, I don't believe that the MMR vaccine causes autism.

Q. At one point there were

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reputable doctors who were opining that it did, right?
MR. DOVEL: Objection. Form.
THE WITNESS: Well, I've never held that opinion. At one point there were some doctors who held that opinion, but I want to make it clear that I've never held that opinion.
QUESTIONS BY MR. MURDICA:
Q. And it -- in your view, it turned out that those doctors that held the opinion that the MMR vaccine causes autism ended up being wrong, right?
MR. DOVEL: Objection. Form.
THE WITNESS: I believe that's true, yes.
QUESTIONS BY MR. MURDICA:
Q. All right. And right now, the opinion you're offering here, Dr. Hollander, is not generally accepted yet, right?
MR. DOVEL: Objection. Form.
THE WITNESS: No, I disagree. So I think that the -- as the evidence is accumulating, I think that more and more individuals and bodies are

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studying this in more detail, and I believe that their opinions are changing, yes.
QUESTIONS BY MR. MURDICA:
Q. Okay. As of today --
A. Yes.
Q. -- right? We're sitting here in August 2023 --
A. That's right.
Q. -- the American College of Obstetricians and Gynecologists disagrees with you as of today, correct?
A. As of today, correct.
Q. Okay. The Society for Maternal-Fetal Medicine, as of today, disagrees with you, correct?
MR. DOVEL: Objection. Form.
THE WITNESS: I believe so.
QUESTIONS BY MR. MURDICA:
Q. Okay. FDA, as of today, disagrees with you, correct?
MR. DOVEL: Objection. Form.
THE WITNESS: No, I don't agree with that. I think that the FDA has evaluated the epidemiology evidence,

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and they've suggested that in order to make a determination, that it's important to be able to study the animal model literature in order to be able to come up with an opinion. And, therefore, they've recommended that animal studies should be conducted and should be funded.
QUESTIONS BY MR. MURDICA:
Q. Okay. And, Dr. Hollander, you may not remember my question, but I'm asking about as of August 2023, the FDA has had numerous opportunities to weigh in on whether the labeling of acetaminophen should be changed to add a risk of ASD or ADHD, correct?
MR. DOVEL: Objection. Form.
THE WITNESS: That's correct, that the FDA has considered the matter with regards to labeling changes.
The FDA has issued labeling changes as it relates to acetaminophen.
So, for example, with intravenous acetaminophen and/or if

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acetaminophen is combined with tramadol, yes, they've changed the labeling as a result of incorporating both the animal data and the human data, yes.
QUESTIONS BY MR. MURDICA:
Q. Do you remember my question, Dr. Hollander?
MR. DOVEL: Objection. Form.
THE WITNESS: Perhaps you can repeat your question if you're not satisfied with my response.
QUESTIONS BY MR. MURDICA:
Q. Sure.
Dr. Hollander, are you aware that many times in the last five to seven years, FDA has been asked whether acetaminophen labeling should be updated in the pregnancy section to include a warning about ADHD?
Are you aware of that?
A. Yes.
MR. DOVEL: Objection. Form.
QUESTIONS BY MR. MURDICA:
Q. Are you aware of a statement

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that FDA made in 2016 that there wasn't enough evidence to do so?

MR. DOVEL: Objection. Form.

QUESTIONS BY MR. MURDICA:

Q. Have you ever seen that?

A. I'm aware. However, I'm also aware of the statement that the FDA has made that in order to make a definitive conclusion, that they would want to look at all of the available data, and that in order to answer the question, they would need to review the animal data.

Q. Okay. And what --

A. And in addition to that, that that work should continue to be done and be funded.

Q. What statement was that, Dr. Hollander? When was that?

A. That was a response to some of their reviews with regard to this matter.

Q. Okay. Was that a public statement?

A. It was a statement that they issued, yes.

Q. Okay. When did they issue that

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statement, Dr. Hollander?

A. Maybe I can look at my materials considered, and then I can go take a look and see when that occurred.

Q. Sure. You can take a couple minutes to do that if you're able to find it.

A. Okay. Well, so I see that there are three relevant documents here. One, the -- well, so I'm looking at the package insert statements that they've issued with regards to Ofirmev and also -- which was -- and then another one with regards to analgesics and antipyretics.

And then I have their regulatory guidelines in 20 -- in January 31, 2023.

And then I also see their background and overview statement in 2009.

Q. Okay. Dr. Hollander, which of those allegedly contains the statement that you just testified to?

A. That -- about the need to look at the data, including animal models and to conduct more animal models?

Q. Sure.

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A. I'll have to take a look at the statements, actually, to determine which one it is.

Q. Okay. But it's your belief that FDA made a -- made a public statement to the effect of what you just testified?

A. Yeah. It's my belief that they've said that in order to answer the question, that they need to be able to incorporate the animal model data in order to make a decision.

Q. Okay. So, Dr. Hollander, you didn't -- you didn't see anything in your review where FDA said that further animal study is unlikely to provide better information?

A. I don't agree with that statement, no.

Q. Did you see that? Did you see that FDA said that?

A. Perhaps you can show me that statement, and then I can respond to that.

Q. Sure.

I'm asking, sitting here today, do you remember ever seeing that?

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MR. DOVEL: Objection. Form.

THE WITNESS: I don't -- I don't remember reading a statement where FDA said that animal data would not inform a decision with regards to this matter. No, I don't remember that.

QUESTIONS BY MR. MURDICA:

Q. Okay. Have you seen FDA's statements this year that it continues to review information regarding acetaminophen and ADHD and ASD outcomes in pregnancy in response to questions of whether the labeling should be changed?

A. Yes. It's my understanding that FDA is continuing to consider the matter and that, you know, as additional information becomes available, both with regards to epidemiology and with regard to the animal models, then FDA may offer additional opinions with regards to labeling changes.

Q. All right. And do you have any doubt that FDA is actually reviewing the information as it comes out?

A. I don't have any doubt that FDA

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would be continuing to review the information. And the information continues to come out, so I know that it's on their radar, and I would expect that they would continue to review information as it becomes available.

Q. Right.

And you have a high opinion of FDA's ability to review information regarding drug safety, right?

MR. DOVEL: Objection. Form.

THE WITNESS: Well, so FDA and pharmacovigilance advisory groups with regards to FDA are responsible for evaluating information with regards to safety and efficacy as it continues to come out.

However -- and in -- this is the history of multiple medications with regards to labeling. As additional information comes out, FDA revises the labeling accordingly.

Sometimes there's a lag time between when the information comes out and when the labeling changes occur,

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but the FDA does incorporate new information and does issue labeling changes to reflect the state of the art with regard to the safety and efficacy. Absolutely.

QUESTIONS BY MR. MURDICA:

Q. And, Dr. Hollander, as we sit here today in August 2023, FDA has not suggested that acetaminophen labeling should say that ASD and ADHD are an increased risk when used during pregnancy, correct?

MR. DOVEL: Objection. Form.

THE WITNESS: Well, the FDA has actually changed the package insert or the labeling with regards to acetaminophen as the new information has come out. And so as I've mentioned, they have incorporated labeling changes for the compound.

One of the issues here is that this is a compound that was developed in the 1890s. It was originally approved by the FDA early 1950s.

In the later 1950s, it went over the counter, so it was no longer

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under the same regulatory considerations from the FDA once it became an over-the-counter product. And at the time that it went over the counter, the practices were very, very different than they are currently now.

But I can say that with recent prescription compounds that include acetaminophen, yes, the label has changed to reflect a more accurate review of the literature with regards to safety and efficacy, yes.

QUESTIONS BY MR. MURDICA:

Q. Are you done, Dr. Hollander?

A. Yes.

Q. Do you think you answered my question?

A. I believe so.

MR. MURDICA: Okay. Would you read back my last question, please, if you can find it?

(Court Reporter read back question.)

MR. DOVEL: Did you want to have that question reposed? Or are

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you just having it read back?

MR. MURDICA: No, I'm having it reposed.

MR. DOVEL: Objection. Form.

QUESTIONS BY MR. MURDICA:

Q. Can you answer that question, Dr. Hollander?

A. Yeah. Perhaps you could restate that question, because I believe that there were a few different components that were included within the same question.

MR. MURDICA: Okay. Would you ask it again, please?

(Court Reporter read back question.)

MR. DOVEL: Objection. Form.

THE WITNESS: Well, my answer would be the same, actually. So that the product labeling more recently for prescription forms of acetaminophen have reflected a change in the -- in the risk versus the benefit or the safety. Specifically now, they're included as a Category C.

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QUESTIONS BY MR. MURDICA:
Q. Dr. Hollander, are you unable to answer the question?
A. The --
MR. DOVEL: Objection. Form.
THE WITNESS: The last question that I just heard, I was answering that question, so --
QUESTIONS BY MR. MURDICA:
Q. Does the acetaminophen labeling today contain anything about autism or ADHD?
MR. DOVEL: Objection. Form.
THE WITNESS: Well, no, the answer is the labeling today does not include anything --
QUESTIONS BY MR. MURDICA:
Q. Okay.
A. -- with regards to ASD and ADHD.
However, I believe that the question that the court reporter just read to me didn't say -- state that, actually.
Q. Okay. We're going to go back and ask it again, Dr. Hollander, and if you can't --

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A. Okay.
Q. -- answer it, we're going to take a break to decide to what to do with the rest of the deposition. Because I'm not going to spend my day having you give nonresponsive answers, because there's better things we can do with our time. So we'll try it one more time.
MR. DOVEL: The witness has been extremely responsive.
MR. MURDICA: Yeah, that's just not -- that's not true.
MR. DOVEL: Please don't interrupt me.
MR. MURDICA: That's not true.
MR. DOVEL: We'll get through today better if you don't interrupt me.
MR. MURDICA: Okay.
MR. DOVEL: Our court reporter is excellent, but she can only write down one person at a time.
MR. MURDICA: I agree.
MR. DOVEL: So let me go ahead and finish my statement.

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MR. MURDICA: Sure.
MR. DOVEL: The witness has been answering directly. I've been posing objections.
I can see the problem with your question. You just can't see the problem with your question. His answers are very accurate.
MR. MURDICA: Wonderful. Thank you. Perhaps on the break you can give me some free advice. But thank you.
MR. DOVEL: I don't give free advice. I'm going to charge you for it.
MR. MURDICA: All right. It ain't worth it.
All right. If you could ask the question that the doctor has been unable to answer one more time, I'd appreciate it.
(Court Reporter read back question.)
MR. DOVEL: Objection. Form.
THE WITNESS: Correct.

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QUESTIONS BY MR. MURDICA:
Q. Okay. Dr. Hollander, are you aware of any medical organizations that as of today, in August 2023, agree with your causation opinion here?
A. Yes.
Q. Okay. And what medical organization is that?
A. Well, the pharmacovigilance committee that advises the European medical -- EMA has offered that opinion. So that is a medical and regulatory advisory group.
Q. Okay. Let's take this one step at a time then.
In the United States, is there any medical organization, to your knowledge, that agrees with the causation opinion you're offering here that acetaminophen causes autism and ADHD?
MR. DOVEL: Objection. Form.
THE WITNESS: Well, yes.
QUESTIONS BY MR. MURDICA:
Q. Okay. Which medical organization in the United States?

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A. The Bauer consensus statement that was published represented a large number of medical experts across different scientific disciplines that explicitly reviewed the literature in 29 different studies and then, based on that, offered specific opinions with regards to safety and efficacy and also with regards to, you know, regulatory guidelines and package insert.

Q. Okay. Dr. Hollander, is the -- are the 91 people who signed the consensus statement, are they their own medical society?

MR. DOVEL: Objection. Form.

THE WITNESS: I'm not sure whether they're incorporated as a medical society. They do represent individuals from a broad range of different medical societies who have scientific expertise and are able to review the literature and offer opinions.

QUESTIONS BY MR. MURDICA:

Q. For example, two of the 91 are members of ACOG and disagree with the 60,000

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that have said that -- that have come out that we agreed earlier do not agree with the opinion, correct?

MR. DOVEL: Objection. Form.

THE WITNESS: Well, I do agree that this is a controversial area. I do agree that different organizations have offered different opinions. And I do agree that opinions do change over time as more evidence accumulates.

QUESTIONS BY MR. MURDICA:

Q. Okay. Dr. Hollander, what United States medical organizations have offered the opinion that acetaminophen causes autism and ADHD in offspring?

A. I'm not sure that I could recall a specific medical organization in the United States.

I do know, for example, that textbooks such as the Briggs textbook, which talks about fetal -- which is the expert reference with regards to fetal medicine and exposure, have modified the guidelines and offered opinions with regards to this matter

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at hand.

Q. Okay. Is Briggs a medical organization?

A. No.

Q. Okay.

A. Briggs is a well-regarded, validated textbook that informs individuals that work with pregnant mothers and doctors who specialize in that, you know, what are appropriate practices with regards to different medicines.

Q. Okay. And, Dr. Hollander, back to my question --

A. Yes.

Q. -- which is, United States medical organizations or societies that share your opinion that acetaminophen causes autism and ADHD.

The answer is, you can't think of one, correct?

A. I can't recall one at this time.

Q. Okay.

A. I can look into that and get back to you.

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Q. Okay. We'll leave a -- we'll leave a blank in the transcript. There are none, but we're going to leave a blank in the transcript --

A. Okay.

Q. -- so you can go back and determine that there are none, and then you can fill it in.

Okay?

MR. DOVEL: No, he's not going to be filling in any blanks.

MR. MURDICA: Well, he asked for it, Counsel.

MR. DOVEL: No, he didn't ask for a blank.

MR. MURDICA: He said he would get back to us. We'll put a blank in the transcript that will remain blank because there are none.

QUESTIONS BY MR. MURDICA:

Q. All right. Next question. You mentioned --

A. Well, maybe just to complete my thought then.

So I haven't -- I haven't

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really considered the matter, and I haven't searched all of the different medical organizations in the United States and haven't determined whether they've offered an opinion on this matter. So I can't really say one way or another because I haven't really considered that question.

Q. Okay. Dr. Hollander, sitting here today, you're not aware of any United States medical organization or society that agrees with you that acetaminophen causes autism and ADHD in offspring?

A. Well, again, I would repeat that I haven't considered the matter, and I haven't searched each of the recommendations for each of the different medical organizations in the United States.

Q. Fair.

But you can't -- I'm sorry, I didn't mean to cut you off. Go ahead.

A. And so I -- to my knowledge at this time, I can't recall one, although I haven't considered that matter. And so it's hard for me to really respond.

Q. Okay. Dr. Hollander, in

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response to a question a moment ago you mentioned a textbook.

Do you remember that?

A. Yes.

Q. Okay. And Dr. Hollander has a textbook as well, right?

A. That's correct.

Q. Okay.

A. Well, no, that's not correct because I have more than one textbook.

Q. Okay. That's a fair point.

How many textbooks do you have that are currently in publication, Doctor?

A. Well, I have two popular textbooks that have had multiple editions.

Q. Okay. And those textbooks contain chapters on, for example, causes of autism, right?

A. Yes.

Q. Okay. And if we looked, would any of your textbooks, any of your chapters, any of the pages in your textbooks today, say that acetaminophen causes ADHD?

A. Well, yes, I believe that the matter was considered in the textbook of

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autism spectrum disorders, and there's about a paragraph that discusses the matter and in particular highlights one of the meta-analysis, the Masarwa meta-analysis, that did suggest an increased odds ratio between exposure, acetaminophen, and outcome, ASD, in that context.

Q. I want you to listen carefully to my question.

If we looked at your textbooks, Dr. Hollander, any of the chapters, any of the pages, would any of them say that acetaminophen causes ADHD?

A. Well, one of the textbooks is on a different area, so it wouldn't be talked about in that text.

But one of the textbooks does relate to autism. If we review the paragraph in that textbook that reviews the literature as of -- so one issue there is that the textbook came out in 2022. Probably was originally written around 2019.

In that particular review, there is one meta-analysis that is cited that raises the issue but doesn't come up with a

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definitive conclusion. It suggests that future work needs to be done and that one might consider the issue of confounders as well.

Nevertheless, they do talk about this issue. They do cite one of the meta-analyses. The meta-analysis does suggest the increased risk between exposure and outcome, but that -- in that particular paragraph, there's no definitive opinion with regards to causation, and they suggest that the matter needs to continue to be studied.

Q. Okay. Dr. Hollander, I take it if you're citing to some particular paragraph, you looked at this recently; is that right?

A. Yes, I have.

Q. In the past 24 hours?

A. No.

Q. Okay. Dr. Hollander, does the textbook -- so I asked a question about ADHD. You're talking about autism. So I'll ask a question about autism.

Does your textbook say that acetaminophen causes autism?

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A. Okay. Then -- so -- and I'm sorry, I thought you had been asking about autism, not ADHD.

I don't believe there are statements with regards to -- or that there's any review, actually, with regards to acetaminophen and ADHD mentioned in the textbook. So the textbooks deal with different issues.

With regard to autism, yes.

Q. It says acet -- okay. I just want to be clear.

Dr. Hollander's textbook says -- published in 2022, right?

A. Well, so it was published in 2022, the material in it.

So one issue with textbooks is that sometimes -- textbooks are a general overview of a particular area. It takes a long, long time for those textbooks to be prepared and integrated. Then you need to have paper shipped from Canada into the United States. There can be long delays in terms of when the material is prepared, let's say, 2019, and when the textbook comes out,

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2022. So sometimes textbooks may not have the most recent information. And as a -- as an overview, they may not have studied all of the information at hand or included all of the available studies or all of the available meta-analyses at that time.

But nevertheless, it is significant that in that textbook, yes, they did discuss the issue with regards to exposure and outcome, and they did cite an important meta-analytic study that reviews the material, but that they make some general statements, well, clearly, you need to consider confounders when you're looking at exposure and outcome and more work should be done.

Q. And, Dr. Hollander, that meta-analysis you're talking about is the 2008 {sic} publication Masarwa; is that correct?

A. No, I believe that's 2019.

Q. 2019. Okay.

Dr. Hollander, my question was, when we open your 2022 textbook, whenever it was created --

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A. Yes.

Q. -- whenever you signed off on what was in it, it does not say the words, "acetaminophen causes autism in exposed babies," correct?

A. I'm not sure it says those particular words.

What I can say is, again, you know, there's about a -- one paragraph. It's a selective review with one meta-analysis. So it's not a comprehensive, deep dive in terms of the available literature or even the available meta-analyses that were -- knew at that time.

One thing that I would also say is that -- so I was overall editor for the textbook, but I also had two coeditors. The particular -- so what we did is we divided up the textbook into different groupings. One of the other editors was the responsible editor for that particular chapter, so I didn't serve as the primary editor on that chapter.

I did serve as the overall editor for the textbook.

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Q. Dr. Hollander, did you review the content of the textbook before you put your name on it?

A. Yes, I -- well, I not only reviewed all of the material, but that I also assigned specific chapters to different editors for them to do specific review as well for certain areas.

Q. Right.

And if you had any question, concern or disagreement with anything in the textbook with your name on it, you could have called, written, asked questions about it to make sure that it reflected your thoughts, what you thought was appropriate, correct?

A. Well, I would say that at that time I hadn't reviewed the literature, I hadn't weighted the evidence, and I hadn't formed an opinion with regards to this matter.

Q. Okay. So in 2019 -- well, you're saying this was -- the 2022 textbook, your testimony is that that's content as of 2019, right?

A. Yeah. Most of the chapters

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were being submitted around 2019, and then it eventually got published at around 2022.

Q. So in 2019, the 2019 content, when we look at what Dr. Hollander said, we're not going to find Dr. Hollander saying -- or his chapter saying that acetaminophen causes ADHD or autism, correct?

A. Well, again, what I would say is that in the chapter, this issue is raised that a particular meta-analysis, the Masarwa meta-analysis, which is a -- is a pooling of data from multiple different studies to look at things like odds ratio in a large sample size, raised the issue.

The authors who did a -- I would say a selective review, not a comprehensive review, said that what -- when you're discussing issues about exposure and outcome, of course you need to consider confounders as well, and additional work needs to be done.

So there was not a statement, that's correct, in the chapter at that time that said APAP, or acetaminophen, causes ASD.

There is a statement that says

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there is literature and there are meta-analyses that suggest that that is a possibility and that additional -- additional literature should be reviewed and additional work should be done to come up with a specific causation opinion.

Q. And, Dr. Hollander, that Masarwa meta-analysis is one of the studies that you say is most important to your opinion that acetaminophen causes autism and ADHD in offspring, correct?

MR. DOVEL: Objection. Form.

THE WITNESS: Well, that particular meta-analysis is an important study. It is one of several meta-analyses. And all of those meta-analyses show a positive association between the exposure and the outcome.

QUESTIONS BY MR. MURDICA:

Q. Do you have, Dr. Hollander, any textbook revisions underway right now?

A. No. Usually that happens when the publishers, you know, contact the editors and they say, well, this has been out for a

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while. We've sold a certain number of books. We think it would be a good -- appropriate time to publish a new edition.

So, for example, I have a textbook on anxiety, obsessive compulsive and posttraumatic stress disorders where we've been through this process, and three different times they've contacted me and asked for an additional edition.

And that did happen in the autism textbook as well, but I have no idea when that might happen again with regard -- I mean, the autism textbook is still relatively new because it was only published in 2022.

Q. Okay. So as of today, you're not working on a new edition of the 2022 Hollander textbook?

A. No.

Q. Okay. Have you attempted to publish this opinion that you now hold, that acetaminophen causes autism and ADHD, anywhere?

A. No.

Q. Are you going to?

A. I don't have any immediate

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plans to do that. It's possible that at some future time I might be asked to contribute to a consensus statement, but I have no thoughts or plans to do that at this point.

Q. Okay. And back to your compensation here.

You're being paid an hourly rate, right?

A. That's correct.

Q. Okay. And what's the hourly rate?

A. My hourly rate is the same as my hourly rate in my clinical practice, which is $1,100 an hour.

Q. Okay. And to date, you've been paid -- or you've charged approximately somewhere in the low six figures for your work here; is that right?

A. I don't believe so. I believe that I've been paid about $76,000 to date.

Q. Okay. And that includes everything through now?

A. Well, no. I've spent hours working on this case in between when my reports were issued and the -- and this

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deposition. So I've put additional time in.
Q. Right.
So at $1,100 an hour, you're going to be over $100,000 by the end of the day for sure, right?
A. I would expect so. I expect that I'd be compensated for the hours that I've put in with regard to the effort, and that -- and my -- I would be compensated at the same rate that I'm compensated for other activities.
Q. Okay. Earlier I asked you about when you expressed in writing that you had an opinion that acetaminophen caused ASD and autism.
Do you recall those questions?
A. Yes, I do.
Q. Okay. And the first time you put it in writing was in your rebuttal report; is that right?
A. That's correct.
Q. Okay. And in your rebuttal report, you purport to do a causation analysis based on human literature, right?
A. Yes. In my rebuttal report,

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you know, I perform a Bradford Hill analysis, so it -- which is a methodology to be able to incorporate the information from the various studies that I've reviewed, yes.
Q. And you just decided, Dr. Hollander, that you should do a Bradford Hill analysis in rebuttal; is that right?
MR. DOVEL: The way that's phrased, that appears to call for privileged information. I'm going to ask you to rephrase that, if you could, so you're not requesting any privileged information.
QUESTIONS BY MR. MURDICA:
Q. Dr. Hollander, you didn't do a Bradford Hill analysis in your initial report; is that correct?
A. That's correct.
Q. And you did in your rebuttal report for the first time, correct?
A. That's correct.
Q. The information that you used for the Bradford Hill analysis in your rebuttal report was available six weeks earlier when you issued your initial report,

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correct?
A. That's correct.
Q. You just chose not to do it the first time, right?
A. No. So I had reviewed all of the relevant information. I had had conversations with other experts to provide additional information. I utilized all of my scientific and medical background and knowledge as well and was able to form an opinion prior to my rebuttal report.
In my initial amended expert report, I didn't have adequate time to perform a weight-of-the-evidence analysis for each of the individual articles that I had reviewed. And because I didn't have time to perform that weight-of-the-evidence analysis for each of the individual studies, I left it out.
Q. Okay. And in your prior expert work, in Abilify, for example, you also rendered causation opinions, right?
A. That's correct.
Q. Okay. And your definition of causation at that point in time was that you

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gather -- you need to have information from a broad range of sources that's all consistent, correct?
A. Well --
MR. DOVEL: Objection. Form.
THE WITNESS: -- consistency is one important characteristic to be able to weight the evidence. It's one of the factors in a Bradford Hill analysis.
QUESTIONS BY MR. MURDICA:
Q. And Dr. Hollander believes, sitting here right now, that the information on acetaminophen exposure during pregnancy and the outcomes of ASD and ADHD are consistent, correct?
A. That's right. In applying the Bradford Hill factors and reviewing the issue of consistency, yes, the available evidence supports consistency.
MR. WATTS: Hey, Jim, we've been going about an hour. Whenever you get to a --
MR. MURDICA: Sure, we can take a break.

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VIDEOGRAPHER: The time right now is 10:51 a.m. We are off the record.
(Off the record at 10:51 a.m.)
VIDEOGRAPHER: The time right now is 11:05 a.m. We are back on the record.
QUESTIONS BY MR. MURDICA:
Q. Dr. Hollander, are you ready to proceed?
A. Yes, I am.
Q. Okay. Dr. Hollander, I take it from your testimony in our last session that you don't believe that the MMR vaccine causes ADHD; is that fair?
A. That's correct.
Q. Okay. You don't believe that the MMR vaccine causes autism; is that fair?
A. That's correct.
Q. Okay. And if I asked you the same questions with regard to thimerosal, does Dr. Hollander believe that thimerosal causes autism or ADHD?
A. Well, thimerosal causes a range of developmental problems. I haven't

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specifically studied in detail thimerosal and ASD and ADHD, but I'm not aware that that's -- well, I haven't -- I haven't studied that issue.
Q. Okay. So sitting here today, Dr. Hollander would not say that thimerosal causes ASD or ADHD; is that fair?
A. I would say it's fair at this time that I don't have an opinion of it, and I don't -- I don't have a belief at this point that thimerosal causes it, but I haven't studied it.
Q. Okay. Sitting here today, does Dr. Hollander believe that SSRIs cause ADHD?
A. No.
Q. Okay. Sitting here today, does Dr. Hollander believe that SSRIs cause autism?
A. No.
Q. Okay. Sitting here today, do you believe that maternal diabetes during pregnancy can cause ADHD?
A. Well, yes, I do believe that maternal diabetes can be a risk factor for ADHD.

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Q. Okay. And if Dr. Hollander is testifying that maternal diabetes can be a risk factor for ADHD, what you really mean is that has a causal role in development of some ADHD.
Fair?
A. I think it's fair that there's elevated risk of the outcome associated with the exposure.
Q. Okay. And by the way, in your -- in your work with patients, are you mostly treating them or are you also trying to determine the cause of their presentation?
A. Well, I would say in a routine clinical practice that, you know, one important role is to help manage the condition and the symptoms that decrease the distress and the, you know, functional impairment. So treatment is an important component, but not the only component.
Q. Okay. And, Dr. Hollander, part of my question is do you seek to identify -- let's say you have a patient that you've diagnosed with ADHD.
Do you, Dr. Hollander, seek to

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identify for the patient the cause of their ADHD?
A. Well, I do seek to identify contributing factors that could either increase the, you know, the distress or impair the functioning. Yes, I do try to determine that and then intervene.
Q. For example, Dr. Hollander, do you send your patients that you've diagnosed for genetic testing?
A. I may, yes.
Q. Okay. Do you do differential diagnoses on the causes of their presentation?
A. Yes.
Q. Okay. And so you know how to do a differential diagnosis, right?
A. Yeah, that's part of my routine clinical practice, of course.
Q. Anything that you consider as a possible -- as -- in the etiology of the presentation of the patient has to be something that you rule in as even capable of causing the condition, correct?
A. Well, there's part of

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differential diagnoses, yeah. You want to consider other conditions or factors that can contribute to the presentation of the illness, and you want to, you know, try to determine whether or not those conditions are playing a role or not.

Q. Okay. So first, you rule in all of the things that could be a potential cause of what you're seeing, right?

A. Well, you consider, yeah, different potential causes or conditions.

Q. And you don't consider causes that aren't potential causes, right?

A. I'm not sure I follow that.

Q. Let me ask a better question.

You just testified that the MMR vaccine can't cause autism, right?

A. Right. I said that the MMR vaccine does not cause autism.

Q. Right.

So you're not going to ask a patient who has autism whether or not they received the MMR vaccine because it's not something that you consider in your differential, correct?

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A. That would be correct.

Q. Okay. And so my question was, the only things you would consider as a possible cause are factors that are actually capable of being causal, correct?

A. Well, I would be interested in causal factors. I'd also be interested in mediators and moderators.

Q. Okay. So you'd put mediators and moderators on your differential diagnosis?

A. Yes.

Q. Okay. And to your knowledge, is that a standard way to do differential diagnosis?

A. Well, if you're going to do a comprehensive differential diagnosis, you'd want to consider those factors.

Q. Okay. Including -- so you would put mediators and moderators as potential causes in a differential diagnosis?

A. No, I wouldn't -- no. So mediators and moderators are not causes. They are factors that can be related to both the exposure and the outcome and can

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influence the effect. Or can mediate or moderate the effect.

Q. Is there a -- well, this question is about ADHD.

A. Okay.

Q. For ADHD, according to Dr. Hollander, is there a presentation of ADHD that's pathognomonic for the cause?

A. Well, there are -- well, there are multiple factors that need to be considered but that there's no single cause for all individuals with ADHD. It's multifactorial.

Q. Right.

And my question was a little different. I was asking whether there's something that's pathognomonic. So let me try asking a better question.

If you see an individual that you've diagnosed with ADHD, can Dr. Hollander say, oh, I can tell by this presentation that it was caused by this one thing?

Do you understand my question?

A. I guess you're saying is there a single factor that can be -- fully account

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for ADHD in a particular individual?

Q. What I'm saying is, is there any particular presentation of an individual that Dr. Hollander says, oh, I know because of exactly how this looks that the cause had to be Y?

A. Right. So you're saying is there like a phenotype --

Q. Right.

A. -- that's associated with a specific cause?

Q. Yes.

A. Well, I think for ADHD and, you know, idiopathic causes of ADHD, there are multiple different factors and cofactors that contribute to the symptoms and the syndrome. So that for most individuals, no, there's not a specific phenotype that's associated with a specific cause.

However, there can be different factors that contribute to the causation, and those factors may differ from individual to individual.

Q. Dr. Hollander, if I asked you that question about autism, would you give me

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the same answer?
MR. DOVEL: Objection. Form.
THE WITNESS: I might give you a different answer in that, you know, with regards to autism, there are known sort of syndromal causes of autism. So those are conditions where there may be a single genetic factor that's associated with a particular phenotype. And then when you look at the phenotype, you can also diagnose them as having ASD because they'd have the criteria.
So in those cases of syndromal forms of autism like Fragile X syndrome or Prader-Willi Syndrome, for example, there may be a single cause associated with the ASD in those particular individuals.
QUESTIONS BY MR. MURDICA:
Q. Right.
So Dr. Hollander could look at a patient with -- a particular autism patient and say, oh, those are the factors that show me that Fragile X is probably the cause,

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let's go get a genetic test.
Right?
A. Well, I think it would be the other way around. So the person may present with the phenotype, then they might get genetic testing, and then that genetic testing would confirm the diagnosis.
Q. Okay. And in that specific example you just talked about, that would be a purely genetic cause, correct?
A. Well, I would say yes and no. And so even in these syndromal forms of ASD like Fragile X or Prader-Willi Syndrome, there's still a lot of heterogeneity in terms of the presentation of the phenotype. So it does differ.
And that there -- there can be factors that modify the presentation of the illness. So even in these syndromal forms of ASD, that there can be other factors that shape the expression of the phenotype.
Q. Dr. Hollander, do you agree that for -- start with autism -- for autism, the more severe the presentation of the autistic symptoms, the more likely that the

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condition is caused by genetics?
A. You know, it's a very interesting question, and I think that the evidence actually points in two different directions with regards to that. So that there is some evidence that the more restrictive you make the phenotype, the stronger the genetic variation or contribution.
However, the opposite is also true because, you know, there are traits actually that run within families, like the broader autism phenotype, that seem to be familial and/or genetic that are actually broader rather than more restrictive aspects of the phenotype.
So it's very interesting because it could work in both different directions.
Q. Okay. And I take it, Dr. Hollander, you don't know how Dr. Cabrera answered that question when I asked him?
A. That's correct, I don't know how he answered that question.
Q. Did you review his report and

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his rebuttal report?
A. Yes, I did.
Q. Okay. Did you see that Dr. Cabrera holds the opinion that the more severe the autistic symptoms, the more likely it is to be caused by genetics?
MR. DOVEL: Objection. Form.
THE WITNESS: I believe that he was responding to a point that had been made by Wendy Chung with regards to that. And I do think that in his rebuttal report he acknowledged that the tighter and tighter the restriction in the phenotype, that there could be more and more sort of genetic heritability.
Whereas if you broaden the phenotype somewhat, then do you have more and more and more environmental heritability contributing factors.
QUESTIONS BY MR. MURDICA:
Q. And do you disagree with him on that point?
A. Well, I do disagree with him with regards to this one idea, which is that

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with regards to the -- so I think it actually can work both ways.

So on the one hand, the more -- the more restrictive you make the phenotype, there can be more genetic heritability. But I also think that you get that genetic heritability even in the broader phenotype, which seems counterintuitive but is also true.

Q. Dr. Hollander, I'm going to ask you some more questions about what can and cannot cause ADHD.

Okay?

A. (Witness nods head.)

Q. According to Dr. Hollander, can a maternal fever -- untreated maternal fever during pregnancy result in a child with ADHD as a cause?

A. Well, yes. I mean, untreated maternal fever, particularly the higher the fever and the longer the period of time, can increase the risk for having neurodevelopmental outcomes, including ADHD or ASD or neurodevelopmental disorders.

Q. According to Dr. Hollander, can

Page 87

maternal obesity cause ADHD in the offspring?

A. Yeah. Maternal obesity, again, can be another factor that increases relative risk for, you know, ADHD as well as ASD and neurodevelopmental disorders.

Q. Okay. Can air pollution, according to Dr. Hollander, air pollution exposure in the mother during pregnancy cause ADHD and autism?

A. There -- I mean, there are studies that suggest that exposure to air pollution increases the relative risk for neurodevelopmental disorders.

Q. Okay. So would Dr. Hollander consider that as a potential cause of an outcome of autism and ADHD in a child?

A. I haven't, you know, studied that in detail, and I haven't, you know, applied either weight of the evidence or haven't looked at the material and then tried to use standardized methodology like Bradford Hill in order to understand causation.

So I -- I'm not -- I can tell you that there is some evidence for an association between, you know, pollution or

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air pollution and neurodevelopmental disorders. There's increased relative risk. But I haven't applied, you know, like a standardized methodology in order to develop an opinion with regards to causation.

Q. Okay. So sitting here today, Dr. Hollander wouldn't be able to tell us whether air pollution exposure to the mother can cause ADHD in the child.

Fair?

A. I think it -- yeah, given that I haven't really applied a kind of a standardized methodology in order to interpret the literature. All I can say is that there's an association, but I'm not sure that I could make a definitive statement about causation.

Q. And not to be tedious, but the same question. Can air pollution exposure to the mother during pregnancy result in ASD in the child, according to Dr. Hollander today?

A. I think I would have the same answer.

Q. Okay. Dr. Hollander, can premature birth cause ADHD in the child?

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A. Premature birth can be a factor that's associated with an increased relative risk of neurodevelopmental outcomes.

Q. Okay. And I think I understand the distinction you're drawing, Dr. Hollander.

A. Yeah.

Q. Are you willing to say that prematurity -- a premature baby, the prematurity itself can be a cause of the ADHD or no?

A. I'm not prepared to offer an opinion in terms of causation, but I can say that there's a -- there's an association.

Q. Okay. And if I asked you -- I'm going to ask you the same question on autism.

A. Right.

Q. Does premature birth cause autism?

A. I mean, I guess my answer is that there's probably an increased relative risk, but that I'm not sure that I could make a comment regarding causation.

Q. Okay. And when I'm asking

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these questions, Dr. Hollander, and you're saying they cause an increased risk but you can't say causation, you would tell me if you believed they weren't possibly a cause.

You're not saying that, right?

A. I'm not -- I'm not saying that they -- I'm saying that, you know, I haven't reviewed the literature and applied standardized methods and looked at things like confounders in order to make a causation statement, yes.

Q. Okay. And just to put further clarity on that. If you were trying to figure out the etiology of autism in one of your patients, for some reason you wanted to do that, and you found out they were born premature, you wouldn't -- you wouldn't rule that out as a cause, right?

A. I could -- I would say that it could potentially be a risk factor, so it could be a contributing factor.

Q. Right.

So you wouldn't -- without more, you wouldn't rule it out. You would consider it on the differential.

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Fair?

A. I would consider it as a factor that could contribute to the -- you know, the outcome.

Q. Okay. Dr. Hollander, low birth weight, can low birth weight cause ADHD in the -- in the child?

A. Well, I would say that a low birth weight is a factor that can increase the risk for ADHD as an outcome.

Q. Does low birth weight increase the risk for autism as an outcome in a child?

A. I believe that that -- that is a factor that has some impact on the relative risk.

Q. Okay. And I don't want to put words in your mouth, but the reason Dr. Hollander isn't saying that low birth weight can cause autism and ADHD is just because you haven't done a Bradford Hill.

Is that what you're saying?

A. No.

Q. Okay. What prevents you from saying that low birth weight can cause autism?

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A. Well, so it's been reported that low birth weight increases the risk for that particular outcome, right?

But in order to determine whether or not the elevated relative risk causes it, you'd have to be able to look at that and establish that it's a causal relationship between the exposure and the outcome.

Q. Okay. And for these things I'm asking about for premature birth, low birth weight, air pollution, you -- it's just that you haven't done that.

Fair?

A. No, I'm drawing a distinction between association and causation.

Q. Okay. And my question, Dr. Hollander, is, I understand you're saying there's an association. Correct me if I'm wrong, but the reason Dr. Hollander can't say that it's causal is because you haven't done a full analysis for causation, right?

A. Well, that's one reason, is that I haven't done a full analysis for causation. And also, I haven't studied the

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literature to determine whether or not there were methods employed to be able to exclude either known or unknown type confounders that may be contributing to the association.

Q. And that's an important part in analyzing an association, to exclude known and unknown confounders, correct?

A. Well, yes. I mean, if you want to determine the relationship between exposure and an outcome, you want to show that that relationship persists even when you do various things to try to control for various known or unknown confounders.

Q. And you can also try to do an analysis to control for bias, right?

A. Right. That -- that's something that you do want to consider. And there are different sources of bias, and you want to be able to control for that bias in multiple different ways.

Q. Okay. Back to the risk factors.

Do you believe that -- does Dr. Hollander believe that difficulty during childbirth can cause ADHD?

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A. Well, again, I would respond that difficulties during childbirth can be associated with an increased risk of the outcome.
Q. And the same question for autism, can difficulty during childbirth cause autism in the child?
A. Well, again, I wouldn't say -- I wouldn't say that. All I would say is that the difficulties in childbirth can be associated with increased relative risk for that outcome.
Q. Dr. Hollander, does maternal hypertensive disorder have the potential to cause ADHD in a child?
A. Well, I mean, I haven't studied that in detail. I haven't -- I haven't really looked at the literature with regards to maternal hypertension.
I know that maternal hypertension in and of itself can be associated with different kinds of negative outcomes, so it is possible that it could be associated with things like birth trauma or premature birth or -- and that those -- so

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it's -- I mean, it's possible that it could be a factor or a cofactor associated with increased relative risk.
Q. Okay. So sitting here today, Dr. Hollander, you can't say whether maternal hypertensive disorder during pregnancy can cause or increase the risk of ADHD in the child?
A. Well, I believe that my response would be similar to the other responses, again, that it -- you know, it may be associated with an elevated relative risk. But, again, because I haven't employed methods to determine whether or not it could be causal, and because I haven't seen whether or not, you know, different sources of bias or potential known or unknown confounders have been adjusted for, it's hard to make a statement with regards to causality.
Q. Okay. And maternal hypertensive disorder, is that preeclampsia?
A. That can contribute to preeclampsia.
Q. Okay. And do you associate preeclampsia with the outcome of ADHD in a

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child?
A. Yes, preeclampsia can be a factor that increases relative risk of the outcome.
Q. Okay. Can preeclampsia cause ADHD in the child?
A. I don't know whether or not it can cause ADHD in the outcome for the same reasons, both in terms of whether or not adequate confounders have been controlled for and the relative risk persists, and also whether or not standardized methodology have been utilized in order to determine causation.
Q. Okay. And, Dr. Hollander, that was about ADHD, and I appreciate the answer. I'm going to ask you the same question about autism.
Can preeclampsia cause autism in a child?
A. That I've -- I think I would have the same response.
Q. Okay. Can childhood eczema cause ADHD, according to Dr. Hollander?
A. Well, childhood eczema, you

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know, can be like a -- you know, an immune inflammatory condition. And immune inflammatory conditions during pregnancy could -- during pregnancy could be associated with things like maternal immune activation, which could be a risk factor increasing the relative risk for the outcome.
Q. Okay. So if I understood you correctly, childhood eczema via inflammation could be an -- be a risk factor for ADHD in the child?
A. Well, let me modify that.
So childhood eczema -- there's an issue of temporality here. So childhood eczema, you're implying that this is something that's occurring in the child post-birth, right? So that wouldn't be a causative factor because of the issue of temporality. It wouldn't occur during the time of fetal development, so that it wouldn't -- it wouldn't -- from a temporality standpoint, it wouldn't be causative.
Q. Okay. Dr. Hollander, from a temporality standpoint, what is the cutoff in development from when a condition can no

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longer cause -- an exposure can no longer cause ADHD or autism?

A. Well, if -- I mean, if you're looking at maternal exposure during pregnancy, and that's the exposure, and the outcome is neurodevelopmental disorders, then the temporality, or the exposure, would occur during pregnant -- pregnancy.

Q. Okay. Let me put a finer point on this.

I think I just heard your testimony that childhood eczema, in other words, after birth, is too late to cause ADHD, correct?

A. Well, it's a -- so I guess -- here is -- here is a caveat, but, yes, in terms of temporality of exposure, yeah, it wouldn't be in the window of maternal exposure, so it wouldn't be associated with a maternal exposure being a...

However, you know, it's possible that, as you know, that, you know, autoimmune disorders can run in families. So if you have a family where there are multiple autoimmune disorders, then it's possible that

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it increases the risk of the mother having a maternal autoimmune disorder during pregnancy. So it could be like a -- you know, a marker.

But -- so one of the ways to determine that is like negative exposures, right? So you look at the temporality of the exposure, and then you look at the exposures outside of that window as a control. So that's why many of these studies have looked at negative exposure four years before pregnancy or four years after pregnancy as a negative control in order to control for that.

Q. Okay. Dr. Hollander, an exposure three months before pregnancy to a medication is not going to cause ADHD or autism in offspring, correct?

A. Well, I would say it would be less likely; however, it's still possible, and I'll give you a possibility.

Let's say the mother was a -- administered a compound that, you know, stored in the fat and persisted for a long time. Let's say the mother was injected with

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a long-acting compound, for example. Then it's possible that the mother would still have measurable, you know, plasma levels during pregnancy.

So in that kind of a case, it could be.

Q. Okay. And so let me put a finer point on my question.

Let's say there's a medication with less than 12 hours of half-life. Exposure three months before pregnancy is not going to affect the fetus, correct?

A. No, I would say if the -- I mean, if you're looking at a longer period of time and a drug with a short half-life, then it would be less likely that an earlier exposure would be associated with maternal exposure unless -- or here's the other -- I mean, just off the top of my head -- unless it was -- unless that exposure beforehand was somehow a marker of the mother's continuing exposure during the pregnancy.

So you might make the argument, well, if somebody is taking something prior to pregnancy, well, maybe there's a higher

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likelihood that it could still be taken during pregnancy. So maybe it would be an indirect marker, but that -- you wouldn't think -- no, for the -- I mean, if it's not -- if it's not in the mother's plasma, it's not a compound that's present during pregnancy, then you wouldn't think that that exposure would be associated with the outcome.

Q. Okay. And, Dr. Hollander, you're not a teratologist, right?

A. No.

Q. But you understand what teratology is, right?

A. Yes, I'm familiar with the principles and practices.

Q. Okay. And do you agree that in general, exposures in the first two weeks of pregnancy are all-or-nothing events that either kill the embryo or don't affect it?

MR. DOVEL: Objection. Form.

QUESTIONS BY MR. MURDICA:

Q. Do you understand my question?

A. Well, I am aware that exposures early on can be associated with higher risks

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of like a termination of the pregnancy, right? So -- and then if the pregnancy is terminated, then you wouldn't have the outcome.

Q. Right.

Do you remember seeing in Dr. Cabrera's report the little chart that showed the first 14 days are exposures that either terminate the pregnancy or don't?

A. I do recall seeing that chart.

Q. Okay. And I guess what I'm trying to get at, Dr. Hollander, is, your window of exposure for something that can cause ADD -- ADHD and autism --

A. Right.

Q. -- is when the mother is actually pregnant up to the time of childbirth; is that correct?

A. That's correct.

Q. Okay. Back to my question on what can cause ADHD.

Can low maternal serum vitamin D cause ADHD in the child?

A. Well, it is possible that, you know, maternal nutritional status can play a

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role as a risk factor for neurodevelopmental disorders and that, you know, nutritional factors that have an impact on things like oxidative stress could potentially be risk factors.

Q. Okay. So would Dr. Hollander consider vitamin D deficiency, a low serum vitamin D, as a potential cause of ADHD in a child?

A. Again, I wouldn't use the word "cause," but I would -- I would say that it's possible that that could be -- there could be a risk factor or an association, and it could be a cofactor.

So poor nutritional status could be a cofactor along with exposure to other compounds that may have an additive effect in terms of impacting the outcome.

Q. And, Dr. Hollander, when you say "cofactor," do you mean it could be a contributing cause to the outcome?

A. Not exactly, no, because -- so contributing cause would be that there would be, you know, multiple hits, and then the more hits that you have, the higher the

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overall relative risk, or the greater likelihood of the expression of the full phenotype.

Cofactors may be things that directly interact then with other factors. So, for example, if you have nutritional -- poor nutrition, for example, or other forms of stress on the mother that could deplete things like glutathione, that could be like a cofactor.

So that, let's say, you have an exposure to a compound that has an impact on, let's say, oxidative stress, but it occurs in a setting where you've depleted a particular antioxidant, then it would be a cofactor. So they would be working in concert together, and they wouldn't just be independent factors.

Q. Okay. So sitting here today, Dr. Hollander would not say that maternal low vitamin D can cause autism or ADHD, correct?

A. Well, for the reasons before, I wouldn't use the word "cause." You know, I might say relative risk or association.

Q. In order to get to causation on

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a question like that, Dr. Hollander, you would need to do a full weight-of-the-evidence analysis, correct?

A. Well, again, you'd want to look to see whether there are other factors that influence the association, right? You would want to -- you'd want to control for other factors that influence the association, and then you'd want to apply standardized methodology in order to determine causation. Yeah.

Q. Okay. And it's just that we -- no one has asked you to do that, right?

So sitting here today, you can't say whether it can be causal.

Fair?

MR. DOVEL: Objection. Form.

THE WITNESS: Well, I guess I'm saying two things. One is, I certainly haven't done that, but I'm also not aware in the literature of that as well or whether others have done that.

QUESTIONS BY MR. MURDICA:

Q. Okay. But you don't know

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whether the literature exists or not, right?
A. I believe that the literature has looked at issues in terms of association, but I don't know whether or not those studies that looked at association adequately controlled for, again, you know, various factors like confounders. And so -- and/or whether or not, you know, anybody has applied standard methodology to determine causation.
Q. Dr. Hollander, have you -- do you have an opinion of whether advanced maternal age can cause autism and ADHD?
A. Well, I do know that there's pretty good evidence, actually, that both maternal and paternal age can be a risk factor for increasing the risk of neurodevelopmental disorders, including ASD and ADHD.
Q. Okay. And paternal age was going to be my next question.
A. Right.
Q. Dr. Hollander, I take it from your answer that the risk factors that -- you haven't done an analysis as to whether advanced maternal or paternal age is

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causative for autism or ADHD.
Fair?
A. Well, I mean, that's a very -- it's an interesting finding. It's a pretty strong finding that has been repeated.
It actually -- it's interesting for a couple different reasons, but one is it informs hypotheses with regards to plausible biological mechanisms as well.
Q. And I understand what you're saying, Dr. Hollander, and I'm just asking. The reason you can't -- you won't say right now that advanced maternal and paternal age is causative of autism and ADHD is because you haven't done a weight-of-the-evidence analysis and looked at it, correct?
A. Well, I think that -- that -- that relationship is pretty strong, that association. And I do believe that there have been attempts to look at different kinds of confounders with regards to that, and that the association persists even when controlling for certain confounders.
I also think that -- again, it's interesting because it suggests that as

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the father or the mother ages, you know, you have sperm or eggs that are replicating over and over and over and over again. And the longer the period of time that that happens, the more likely that you can get problems in terms of, you know, copying the DNA, and you're more likely to get de novo mutations, actually.
So, I mean, it's a very interesting idea that as a -- as an environmental factor, I guess, maternal or paternal age, it actually can influence the genetic contribution.
Q. And understanding, Dr. Hollander, that you're, you know, considering this right now --
A. Yeah.
Q. -- are you willing to say it's causal today or not?
A. I'm not able to say whether or not it's causal today.
Q. Okay.
How about maternal depression, Dr. Hollander? Is maternal depression causative of ADHD in the child?

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A. Well, I think it's well-documented that, you know, maternal stress and maternal psychiatric illness is not good for the baby or the fetus. However, I think that that's an area where people have looked at different kinds of confounders and tried to control for that, and there hasn't been strong evidence for causation.
Q. Do you recognize, Dr. Hollander, that there's an association in studies between maternal depression and the outcomes of ADHD and autism?
A. I'm aware that there's an association. I do know that people have been trying to blame the mother for long periods of time on causing autism, the whole refrigerator mother hypothesis. And that's been carried forward also to look at various kinds of maternal behavioral factors and psychiatric factors and looking at their relationship to outcome.
Q. Dr. Hollander, you raise a good point. There's been several things that have been blamed as causes of autism that turned out to not be true, right?

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A. That's true.
Q. Okay. One of them is what you just mentioned, refrigerator mothers, the theory basically that the mothers were cold and didn't love their children and they developed autism, right?
A. That's correct.
Q. Okay. And that -- you agree that is not something that is factual, right?
A. No. So refrigerator mothers are not the cause of autism.
It is possible that, you know, profound deprivation, so people who are like raised in orphanages and don't get any kind of maternal caring, can be at increased relative risk for developing neurodevelopmental problems. But, no, that, you know, refrigerator mothers don't cause autism.
Q. Right.
And, Dr. Hollander, there was a point in time in the early 20th century when doctors actually said that was a cause of autism, right?
A. That's true.

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Q. Okay. And we discussed this earlier, but there was a point in time only 20 years ago when some doctors thought that vaccines caused autism, right?
A. That's true. The theory has been discredited, but there was a time when some people posited that.
Q. Yeah.
And, Doctor, to make this easier, I'm going through things that have been attributed as causes that have been discredited --
A. Okay.
Q. -- and seeing what you agree.
A. Okay.
Q. Have you -- do you know that the Ferber method of --
A. Yeah.
Q. -- with children has been discredited as a cause of autism after being attributed as a cause?
A. Yeah, I agree that the Ferber method doesn't cause autism.
Q. Dr. Hollander, are you aware that there were theories with doctors saying

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that certain dairy products caused autism?
A. I am -- I am aware that some people feel that like a, you know, gluten and casein-free diets, for example, that those can trigger inflammatory processes. And so one approach is try to eliminate that, for example, in the diet and see whether or not it affects behavior.
Q. Okay. Does Dr. Hollander believe that the dairy products and gluten theory as a cause of autism has been discredited?
A. Yeah, I think there's no evidence that that causes autism.
Q. Okay. Have you seen, Dr. Hollander, that there was a theory posited by doctors that modern wheat, the advent of modern wheat, was causing autism?
A. Well, the same idea again, you know, like wheat can trigger inflammatory processes in some people who are sensitive to that. But I don't think that wheat is the cause of autism.
Q. Okay. And cable TV was posited as a cause of autism.

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Are you aware of that?
A. I'm not aware of that.
Q. Okay. Dr. Hollander, cable TV is not a cause of autism, right?
A. No.
Q. See, the easiest question in your deposition.
A. Okay.
Q. Okay. Let's talk a little bit about the diagnosis rates of autism and ADHD.
Dr. Hollander, in your rebuttal report, at one point you say they're increasing, and at another point you're saying they're stable throughout the world.
What is your opinion right now about the diagnosis rates of ADHD and whether they are increasing, decreasing or staying flat?
A. Well, I disagree with your statement that in my rebuttal I state that the rates of ASD and ADHD are stable throughout the world. I believe that I was referencing a comment that Dr. Faraone said. So that's where that sentence came from. It wasn't from me.

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Yeah, I believe that in the last 20 years, you know, the rates of ASD have more -- they have quadrupled. So like a 400 percent increase. And so the rates have gone from about 1 to 350 to 1 in 36.

Q. You're talking about autism, Doctor?

A. Autism, yeah.

Q. Okay. And, Doctor, in the opinion of Dr. Hollander, does that represent an autism epidemic or just better diagnosis?

A. Well, that's a good -- it's a good question, and that is a topic that has been debated in the field, whether the increase in estimates, let's say, from 1 in -- just in the last 20 years, 1 in 350 to 1 in 36, can be attributed solely to, you know, broadening diagnostic criteria or increased public awareness or greater screening, for example, or whether, in fact, they represent true increases. And there are different ways to try to disentangle or address that.

So one of the ways to try to address that is to use standardized

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surveillance methods in a prospective fashion that occur at frequent intervals. So that's an approach, for example, that the CDC uses. They use standardized methodology at regular intervals with valid, reliable outcome measures.

In addition to that, you can look at sort of medical diagnosis rates from electronic medical records, things like that. So you're having a standardized methodology applied at regular intervals over time in order to determine, you know, prevalence rates.

There you see, you know, that the prevalence rates are increasing using the same assessment measures and the same methodology in a prospective fashion at regular intervals, and that you get the -- you get similar kinds of rates, or you get similar increases in rates, with different methods, whether you're looking at electronic medical records and clinician diagnoses or whether you're using other sampling kind of techniques.

Q. Okay. I appreciate that,

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Dr. Hollander, but what is your opinion? Is your opinion that -- we'll start with autism -- that there are genuinely more cases of autism, and it doesn't have to do with the other potential explanations that you just said?

A. Well, my opinion is that there are different factors that can contribute and that need to be understood and controlled for.

Q. Okay.

A. So I am aware that diagnostic criteria have changed a little bit, you know, particularly with the idea in DSM-5 of looking at the spectrum as opposed to individual diagnoses, and I am aware that there's a lot more awareness now of these conditions.

And I'm aware that there's more routine screening for those conditions as well, and then I am aware that there's more referral to specialists. So those things are all true.

However, I'm also aware that using standardized methodology and different

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approaches, you know, the rates continue to increase. And so I believe that while some of those factors may contribute to some extent, there's still a significant increase even when you control for all of those other kind of factors.

Q. Dr. Hollander, do you believe the same thing for ADHD? Because you were asked -- answering about autism.

A. I was answering for autism.

And I think with regards to ASD, you know, the results are a little bit different.

Q. ADHD. I don't mean to interrupt you, but you said ASD.

A. I'm sorry. I apologize.

Q. We're talking ADHD.

A. Yeah. Right.

Q. I just want to save you from having to repeat it.

A. No. Well, yeah. I do believe that the rates for ADHD have increased over time, not as dramatically, but there has been an increase, and that I -- that represents an increase in the true prevalence and --

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although there could be other factors that, you know, contribute to the diagnosis.

Also, the same answer. Using standardized methods and different approaches, there's still a significant increase in rates over time.

The time -- the time span is a little bit different. So the time spans that are kind of measured, in ASD you have a nice period of 20 years where you can sort of measure that using standardized methodology.

Here, the time intervals are a little bit different, but the finding is similar, that there's an increased rate, even if you account for awareness and screening and diagnostic changes and, you know, other kinds of factors like services and things like that.

Q. Okay. Dr. Hollander, let's go through some of those factors.

So with respect to ADHD, the diagnostic criteria did, in fact, expand quite a bit, right?

A. Well, there were some changes, for example, with regards to age of onset.

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Q. 7 versus 12, right?

A. Correct.

Q. Okay. So you went from having diagnoses for people who had symptoms before 7 to including five more years, anybody who had symptoms before 12, right?

A. That's true. That is a change.

You know, part of the reason for that is that there was a significant underdiagnosis of individuals with adult ADHD. And so it didn't really represent the true prevalence of adult ADHD because there was this artificial cutoff. And when you expand the, you know, onset of presentation, you may get a more accurate presentation.

And that's particularly true for -- so one of the issues is people have the inattentive, you know, subtype. There's a large, I guess, misidentification. Those individuals may not be -- if you're not exploding or having temper tantrums, you're not impulsive, you're not hyperactive, you're less likely to be picked up, right? So it may present in adulthood.

And then if you have an

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artificial cutoff where it demands that it's identified by a certain age, then you may be minimizing the illness.

I mean, the second issue is gender issue. So ADHD is much less likely to be picked up in women, partly because women have less, you know, disruptive behavior, temper tantrums, irritability, hyperactivity. And therefore, again, you know, there's an underrepresentation.

And so I think it's a step in the right direction by including a different age cutoff because it gives you a more accurate representation.

But nevertheless, you're right, there was a change in that diagnostic criteria.

Q. And that increase -- and that resulted in a significant increase in the number of diagnoses in the United States, correct?

A. It did identify many individuals who hadn't been diagnosed prior to that because of that cutoff.

Q. Right.

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And so you would agree with me that that change, the change from 7 to 12, greatly increased the diagnoses of ADHD in the United States, correct?

MR. DOVEL: Objection. Form.

THE WITNESS: Well, I would say that, you know, it's certainly possible that that could be a factor that could alter, you know, diagnostic rates.

However, you know, one of the things that I would say, though, in the ADHD is at the time -- so the -- 2013 was when DSM-5 was published, right? And that the surveillance techniques in ADHD were often for relatively time -- shorter time periods. So you could -- I mean, you could specifically control for that by looking at, you know, rates. Rates after 2013, you know, the criteria would be the same.

QUESTIONS BY MR. MURDICA:

Q. What's the average age, Dr. Hollander, of the diagnosis of ADHD in

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the United States?
A. Well, you're raising a good point in that, you know, the longer the follow-up, the higher the number of individuals that you're going to be picking them up.
I think that patients -- I guess it varies. Again, the hyperactive, impulsive individuals are going to be diagnosed much earlier, and the inattentive subgroup are going to be diagnosed much later. The girls are going to be diagnosed later. So that there are different factors that influence age of onset.
Q. Yeah.
And do you know the average age of diagnosis, Doctor, in the US?
A. I think often, you know, the diagnosis can be made, you know, by around age 7, but there are many -- you know, many people who don't present until after -- until 12. I mean, that's why the diagnostic criteria have changed.
Q. What's the average age of diagnosis of autism or ASD in the United

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States?
A. The age of onset with autism, again, really varies based on the presentation. So you've got kids who are, you know, aggressive and having temper tantrums. They're going to be diagnosed at a much earlier age.
Girls are going to be diagnosed at a much later age.
Those individuals with high IQ, those would good verbal ability, are going to be diagnosed at a much later age.
So the -- and now we're finding that, you know, more and more people who are higher-functioning and who have good verbal skills are really not diagnosed until adulthood, actually.
Q. And --
A. So it depends on the -- it depends on the phenotypic presentation.
Q. I understand that, Dr. Hollander. And all I'm asking is, do you know the statistic in the United States of the average age of diagnosis of autism?
A. Well, then, again, it depends

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on the cohort, the racial and ethnic group. And so there are a lot of different factors that influence it.
I could say that kids are often diagnosed -- you know, truthfully, the -- well, you have two different factors competing. One is more screening and early diagnosis, but then the idea that -- you know, you're picking up more individuals with milder forms, so it's working in two different directions. But it may be around -- and it -- definitely there are big factors in terms of racial and ethnic and socioeconomic factors.
I would say maybe like around age 5, but it really varies. Some people are being picked up at 18 months, and some people are picked up at adulthood.
Q. Right. And I understand all of the qualifiers, Dr. Hollander.
But in general, you would -- you would testify here that if you factor in everybody who has a diagnosis, the age of diagnosis on average for ADHD across all the different populations is about age 7, and for

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autism across all the different populations and given all those caveats is around 5.
Fair?
MR. DOVEL: Objection. Form.
THE WITNESS: I would say that those estimates are roughly appropriate. And I'll also say that the age of onset of ASD tends to be before the onset of ADHD.
But I would also say there are so many different -- it really depends on the cohort that you're measuring it in because it can vary.
QUESTIONS BY MR. MURDICA:
Q. And, Dr. Hollander, one of the other reasons that the diagnoses -- the number of diagnoses are increasing in the United States, I think you mentioned earlier, but more awareness by medical providers to look for these symptoms in women, right? In female children?
A. Well, I agree, without a doubt, there's been an underdiagnosis in women for a number of different reasons. So, you know, in -- so in ASD, there's a 4 to 1 ratio.

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Maybe that's not really an accurate ratio, and maybe -- and some have suggested a more recent kind of approach is that the ratio could be lower than that.

And so I -- as I mentioned before, you know, women tend to get underdiagnosed. And in particular, you know, women who have verbal ability and are not exploding, they're much less likely to be diagnosed, and they're much more likely, if they're going to be diagnosed, to be diagnosed at a later age.

I can tell you that I have a lot of women in my practice who were not diagnosed until adulthood, actually, and they were given other diagnoses prior to that.

Q. Dr. Hollander, with respect to ADHD, there used to be a similar large imbalance between the sexes, and now it's almost close to parity, isn't it -- is it not?

MR. DOVEL: Objection. Form.

THE WITNESS: Well, I would agree that, you know, there was a higher male-to-female ratio, and I

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would agree that over time that that ratio is narrowing as more women, particularly with those with the inattentive subtype, are being picked up.

QUESTIONS BY MR. MURDICA:

Q. And you said earlier in one of your answers, I believe, that another reason for increasing diagnoses are the availability of services, right?

A. That's correct.

Q. Okay. In 2004, the IDEA was passed which had a -- it was a significant benefit for children with autism and ADHD diagnoses in school in terms of not being separated from classes and getting the same quality of education with their diagnosis, correct?

A. Well, I would agree that there are different purposes or uses of a diagnosis. And I would agree, for example, in the case of autism that getting an autism diagnosis can be associated with the ability to obtain certain services, yeah.

Q. Services, Doctor, that were not

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available 30 years ago, correct?

MR. DOVEL: Objection. Form.

THE WITNESS: Well, I mean, I would say that -- services that may not have been accessible. They may have been available, but people may not have had as much access to those services.

QUESTIONS BY MR. MURDICA:

Q. Okay.

A. But things like, you know, behavioral therapies and occupational therapy, speech therapy, those were -- those were around for a long time, but having a diagnosis can impact the ability to get services.

Q. And services have become more available through school districts with increased awareness over time, right?

There's more services available with a diagnosis now than there was a decade ago; is that fair?

A. Yeah, I would say that there are more services available now than 20 years ago.

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Q. Okay. And let's see if you can agree on some other things that a diagnosis -- that a diagnosis changes.

If you get an ADHD diagnosis now, a student in school will get extra time on tests, right?

A. That's true, you can get some accommodations with a diagnosis.

Q. Right.

And one accommodation is extra time on testing, right?

A. That's correct.

Q. One accommodation is extra time on standardized testing like the SAT, right?

A. You may be able to get that, although there are a lot of hurdles that you have to go through in order to actually obtain that. But that's true.

Q. Okay. In fact, you can actually get SSI with a diagnosis in some -- in some cases, right?

A. Well, you know, if you have a neurodevelopmental disorder and you're disabled, you can get benefits.

Q. You can get private tutors from

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the school district with a diagnosis, correct?
A. You can get services.
Q. You can get individual education plans, IEPs?
A. Yes, with a diagnosis.
Q. Okay. Any other services you can think of?
A. Well, there may be -- I mean, people definitely can benefit from executive function coaches, for example. There may be some socialization-type services that you can also get.
Q. Are you familiar with IDEA, the congressional act?
A. Yeah.
Q. Okay. Are you familiar with the change in rate -- change in number of diagnoses following the passage of that act?
A. I haven't looked at the timing and the impact of the timing on the slope of the rates.
Q. In your report, you were only looking prior to about 1996, right? In terms of the change in diagnosis rates of autism?

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A. Well, in my report, for example, I also had a figure from my California ecological study that looked at rates over longer periods of time.
Q. Okay. And I'm talking about the US diagnosis rate. The cutoff of what you looked at went to about the mid-'90s, right?
A. I don't recall. Maybe you could -- if you're talking about a specific aspect in my report, you could point me to that --
Q. Sure.
A. -- and I can comment on that.
Q. And we'll do that after lunch.
A. Okay.
Q. Do you know --
A. But I -- but I -- but I did cite in my report studies in the state of California that looked at the rates over really extended time periods.
Q. Okay. Do you know nationally what -- do you know what year IDEA was passed?
A. Not off the top of my head.

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Maybe you could inform me.
Q. 2004.
Do you know what happened to diagnosis rates after 2004?
A. We could take a look at some figures.
Q. Sitting here today, you don't know if it changed dramatically, right?
A. I haven't reviewed figures. I'd be interested in looking at those figures and then looking at 2004 to see how that particular -- because there are various -- so there are a lot of different things that have happened that may have some impact one way or another in terms of rates of these conditions.
And I think you could point to a range of different -- so I would point -- I think one important time period would be the rate that doctors put warnings on ibuprofen with regards to maternal usage and the timeline of those different warnings which influenced, you know, the exposure rates, and then look at those changes in the exposure rates and then how they relate to outcome

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rates.
Q. Right.
A. So there are a lot of different things that you could look that could potentially have some influence on outcome rates.
Q. One of the things you pointed to, Dr. Hollander, in your report were the Tylenol murders in 1982, right?
A. Yeah.
Q. And your theory is that the publicity around the Tylenol murders in Chicago in 1982 nationally caused pregnant women to stop using acetaminophen, correct?
A. Well, yeah, I mean, the -- I guess the public awareness about, you know, that particular contamination or outcome influenced the usage, right? And that would be something to look at. So that would be something that would affect exposure. And then you want to see whether a change in exposure affected a change in outcome.
Q. Right.
So you would want to see, Dr. Hollander, if, following the Tylenol

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murders in 1982, if the autism diagnosis rate went down five years later at about the average time of autism diagnosis, correct?

A. Well, five -- I mean, I would probably want to look at it in a broader range than just five years, to tell you the truth, because, again, people can present at different ages.

Q. Right.

But we're talking about averages, right? You're looking at statistics overall. You want to look at the average, correct?

A. I guess you'd want to look at the mean and maybe the median, so there are different ways to look at it.

Q. Okay. And if we were looking at whether the Tylenol murders had an impact on the ADHD diagnosis rate, we'd look a little further out, more like six or seven years, like you said, right, Doctor?

MR. DOVEL: Objection. Form.

THE WITNESS: Well, it would be the same caveat again because there are a lot of nuances in terms of

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presentation, and those nuances depend on the cohort that you're looking at.

So...

QUESTIONS BY MR. MURDICA:

Q. Okay.

A. But -- but there would be some time association, but it could be depending on what are the cohorts that you're measuring it in.

Q. Doctor, on average, if we're looking at autism rates in 1984, we're really looking at births in 1979, 1980, correct?

A. Well, that would be the case if we assume your average of five years and you're talking about ASD, right?

Q. I'm talking about ASD, yeah.

A. Okay.

Q. If we're looking at autism diagnosis rates in 1984, we'd really be talking about children born in 1979, 1980, on average, correct?

A. Again, but with the same, you know, caveats in terms of the average.

Q. Okay. What do you know about the benefits offered to Cuban citizens for

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different neurodevelopmental diagnoses?

A. I would imagine that the benefits in Cuba are not identical to the benefits offered in the United States.

Q. Do you know anything about the benefits offered in Cuba?

A. Well, I do know that, you know, Cuba is a Third World country, and so -- and, you know, a much poorer country with less access to various kinds of services.

Q. Do you think there would be -- do you know if there's any stigmas attached to having a diagnosis like autism in Cuba?

A. You know, there's a good point because -- so then you have these two sort of competing issues, so stigma versus, you know, benefits, for example.

Yeah, I do think that there are differences with regard to cultural factors and stigma.

Q. And you haven't done any analysis on why and how autism is diagnosed or not diagnosed in Cuba, have you?

A. You know, I've read things that allude to that. You know, I haven't studied

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it in detail, you know. It's clear that there's less services available, and so there's probably less screening and referral and access to different kinds of services.

Q. Let me -- let me put this simply, Dr. Hollander.

Is it really -- is Dr. Hollander really relying on diagnosis rates in Cuba to render your causation opinion here that acetaminophen can cause ASD and ADHD?

A. No, I'm not relying on --

Q. Okay.

A. -- diagnosis rates in Cuba --

Q. Okay.

A. -- to support my opinions here.

MR. MURDICA: When do you guys want to do lunch? I can take a break now or move to another area.

MS. HEACOX: I think it's going to be delivered at 12:30, supposedly.

MR. MURDICA: Okay.

MR. DOVEL: So let's keep going until 12:30.

MR. MURDICA: Let's keep going.

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QUESTIONS BY MR. MURDICA:
Q. All right. After lunch we're going to mark your rebuttal report, but I'm going to ask you some questions about it now. We'll see if you can answer them without it. If not, we'll move on to something else.
In your Bradford Hill analysis, one of the factors you looked at was temporality.
Do you remember that?
A. Yes, I do.
Q. Okay. And temporality -- you ascribed, you say in the rebuttal report, that you put great significance on the satisfaction of that element in your analysis.
Do you recall that?
A. I do.
Q. Okay. And the only thing required to satisfy temporality, according to the analysis in your report, is that the exposure occurred before the birth, right?
A. Essentially, yes.
Q. Okay. So Dr. Hollander, isn't that -- isn't that really a yes or no and not

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a great or limited significance?
A. Well, look, if we're talking about exposure and outcome, and that's what we're talking about, and we're talking about maternal exposure, yeah. So then, yeah, the exposure has to occur during the maternal period.
Q. Right.
But it's not like there's anything unique about acetaminophen exposure compared to other exposure for this factor, for temporality, correct? Any exposure before the birth you're counting as satisfied, fair?
A. Yes. I mean, there are all these nuances in terms of how you measure exposure. But, yes, with regards to just the issue of temporality, yeah, that the exposure had to occur during pregnancy.
Q. One of the other things you say in considering your Bradford Hill analysis is that you're looking at results that were statistically significant, right?
A. Yes.
Q. Okay. And you know what

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statistical significance is, correct?
A. Yes.
Q. And statistical significance is important for you to identify a relation -- a causal relationship between an exposure and an outcome, right?
A. Statistical significance is important as one of the overall factors in terms of how you determine, you know, the strength of the association between exposure and the outcome, but it's not the only factor.
Q. Right.
A. And so you'd want to look at confidence intervals, for example. You'd want to look at consistency of findings. You'd want to look at reproducibility or replication. But statistical significance is important.
However, you know, you can still determine causation without statistical significance, but it's one important factor. But you'd also want to look at, you know, confidence intervals, and you'd want to look at consistency, and you'd want to look at

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replication, and you'd want to look at, you know, whether multiple different studies showed the same, you know, direction.
So whether it's a positive association or whether it's a negative association, you look at all of that. You weight all the evidence, and then that can help to determine causation.
Q. Dr. Hollander, isn't -- aren't the confidence intervals how you define statistical significance?
A. The confidence intervals don't exactly map onto the p-value. So they're two different sort of measures of strength of association.
Q. Okay. For a point estimate to be statistically significant, the confidence interval has to be entirely over 1, correct?
A. Again, not necessarily. So, again, like when you're looking at the totality of the evidence, what you want to do is, yeah, you do want to look at the confidence intervals.
However, you know, even if in an individual study the confidence interval

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may be below 1, you know, if it's a positive association that occurs over and over and over again, then it wouldn't be disqualifying or troubling to have an individual study where the confidence interval was below 1.

Same thing as the p-value. I mean, you want the p-value to be less than .05. You'd want there to be a -- but you'd also want there to be, you know, a positive association that occurs over and over again in the same direction with replication. Then it may be that there are some studies that don't reach a p-value of .05, but -- so you want to look at the totality, really, in order to understand the association that informs causation.

Q. Do you think you answered my question?

A. I think so. I think the answer is, it depends. So you can -- you can have causation even if the p-value in some cases is greater than .05, and you can have causation even if you have some studies where the confidence interval is less than 1, yes.

Q. Okay. My question was this.

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Let's try it one more time.

For a point estimate to be statistically significant, the confidence interval has to be entirely over 1, correct?

A. Generally that's the case.

Q. Okay. And statistically that's the case, right? That's the very definition in statistics, correct?

A. I would say that that -- that is generally the case for a single-point estimate.

Q. And that was my only question.

A. Okay.

Q. All right. For a p-value to be important to you, does it need to be .05 or less?

A. No.

Q. Okay. What p-value matters to Dr. Hollander?

A. Well, we also look at trends. So, you know, a trend can be -- even if the p-value is greater than .05, you may have a trend. It really depends on the sample size.

So, for example, in preliminary studies, when you're trying to understand an

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association and you're trying to do a power analysis, you're looking at the effect size. The thing that's most important is the size of the effect and not the p-value.

Q. Okay.

A. And then you take that information, and then you can use that information to design studies of adequate sample size.

So you can have a trend that's very important. You can establish an odds ratio or an effect size, and then you can utilize that information. That could be very valuable even if the p-value is greater than .05.

Q. Is there a p-value that statisticians generally consider to be the target p-value to find an association?

A. Well, there are some general assumptions, and then there are -- certainly there are some occasions where the association is very important. It gives you critical information, even if the p-value is greater than .05.

Q. Yeah.

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And --

A. So you want to -- again, like one example again is that if you have studies over and over again that show the same positive association, the same direction, the same trend, even if you have a p-value than -- that's less than -- that's greater than .05, then it -- then it provides very important information.

You can still include that, for example, in meta-analyses. And then when you pull the data with a bigger sample size, then you -- so the P -- the p-value is simply influenced by the sample size, right? That's the nice thing about meta-analyses. You can pull the data that shows an effect and establish a much bigger sample size. Then that can give you a much stronger p-value.

Q. Dr. Hollander, my question was this: Is there a p-value that statisticians generally consider to be the target p-value to find an association in a given study?

A. Well, there's a general assumption that P equals less than .05 --

Q. That's all I was asking.

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A. -- is a strong association. But again, it all depends on the sample size. So the p-value is influenced by the sample size.

What you -- any information that you gain from that determine -- is determined by the design of the study. So if the -- if the study has an insufficient sample size, it may give you a p-value that's greater than .05. And then you need to interpret that with regards to interpreting the study.

You say, well, all right, so that particular study has a low sample size. Let's see what happens if we pull the data from different studies with a low sample size, so all of a sudden we have a bigger sample size. Then that's going to give you a different p-value.

Q. You're talking about a meta-analysis --

A. That's an example.

Q. -- in that example, correct?

A. Yeah, that's an example of that.

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But you can pull data outside of meta-analyses as well, so --

Q. In a single analysis, in a single study, is it accurate, based on what you just said, that generally the target p-value is something less than .05, Dr. Hollander?

A. Well, I think my answer again is usually in a single study, generally the goal, if you want to disprove a null hypothesis, is to obtain that. But the study is only good -- it's only as good as the design of the study, right? So that there are various issues in terms of the study design that you need to evaluate in order to judge the value of a particular study.

So, you know, again, you know, for pilot studies, we don't even pay attention to the p-value. We're much more interested in the effect size rather than the p-value. And then we use that strength of the association based on the effect size then to power additional studies, for example.

Q. Dr. Hollander, did you attempt to do a disproportionality analysis here?

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A. I attempted to evaluate the data, understanding the design of the different studies and controlling for various forms of confounders or bias and using standard methodology in order to interpret that.

Q. You know what EB05 is, right?

A. Yes.

Q. And in fact, in another litigation you did a disproportionality analysis to determine causation, correct?

A. It's possible that I did that analysis.

Q. And the EB05 is the important part of the disproportionality analysis to show the association, correct?

A. Well, no. I mean, I think you -- there are different ways to -- there are different types of analyses, and it depends on the association that you're looking at.

Q. Okay. Here, for acetaminophen and ADHD and autism, did you do a disproportionality analysis?

A. I don't believe that I did a

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disproportionality analysis --

Q. Why not?

A. -- here.

Q. Why not?

A. It depends on the -- so, for example, each -- there are significant differences in each individual case in terms of the compound, in terms of the reporting and the data available in order to do that type.

One issue here is that acetaminophen has been on the market for a long time, and it's an over-the-counter medicine as opposed to a prescription medication. So that there may be data available from prescription medications where you can do certain analyses. When you're looking at effects on over-the-counter medication, you may not have access to all that kind of information to be able to do all those analyses.

Q. Did you ask for that information here?

A. You know, the problem, I guess, here is that the vast majority of individuals

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who were taking acetaminophen are not taking it as part of a prescription product.
Q. Did you ask for the information, if it's available?
A. I didn't ask for the information, if it's available. However, unfortunately, I think it would be less relevant because the majority of the exposure is occurring with over-the-counter usage.
MR. MURDICA: Okay. It's 12:30. Do you want to take our lunch break?
MR. DOVEL: Let's go off the record and talk about that.
VIDEOGRAPHER: The time right now is 12:30 p.m. We are off the record.
(Off the record at 12:30 p.m.)
VIDEOGRAPHER: The time right now is 1:04 p.m. We are back on the record.
QUESTIONS BY MR. MURDICA:
Q. Dr. Hollander, welcome back.
A. Welcome back.
Q. Are you ready to proceed?

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A. Yes, I am.
Q. Okay. Earlier this morning, I asked you about your website for Spectrum Neurosciences.
Do you recall those questions?
A. Yes.
Q. Okay. And I asked if we looked, if it would say anything about you and ADHD.
Do you recall that?
A. Yes.
Q. And you said it would, right?
A. Yes.
Q. Okay. Do you hold yourself out as an expert in ADHD?
A. Yes.
Q. Okay. And have you diagnosed causes of ADHD in your patients?
A. Yes.
(Hollander Exhibit 51 marked for identification.)
QUESTIONS BY MR. MURDICA:
Q. I'm just going to mark this as 51.
Dr. Hollander, do you -- sorry.

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Do you recognize that as your bio?
MR. DOVEL: Objection. Form.
THE WITNESS: Well, I recognize that this is a description of me that's on that website.
QUESTIONS BY MR. MURDICA:
Q. All right. And this is your website, right?
A. This is one of my websites, yes.
Q. Do you see anything about ADHD on here?
A. Well, I see information here about impulsivity and aggression and other specific impulse control disorders like gambling. So that ADHD plays a fundamental role in all of the impulse control disorders and impulsivity and aggression.
Q. Okay. Dr. Hollander, your bio on Spectrum Neurosciences doesn't say attention-deficit/hyperactivity disorder, correct?
A. Well, as I recall on the website, yes. You know, there is a description of our expertise with regards to

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attention-deficit/hyperactivity disorder.
Q. Yeah, and I'm asking specifically about Exhibit 51 in front of you --
A. Right.
Q. -- your bio on your website.
We can look and look and look, but we're not going to see ADHD in this text, correct?
A. No, I see -- I see we're talking about issues around impulsivity, which are fundamentally tied to ADHD. And I recall that there's a good description, actually, of ADHD and our overall services and what we focus on on that particular website, but I don't see ADHD listed on this particular bio.
Q. Dr. Hollander, what -- you mentioned that this is just one of several websites.
What other websites do you host?
A. Well, we also have a website for the autism/obsessive compulsive spectrum disorders program at Albert Einstein College

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of Medicine and the Montefiore Medical Center, and also the fellowship program as well on autism and obsessive compulsive spectrum disorders on the Einstein and Montefiore website.

And then there's also a website on the Spectrum Neuroscience Research Foundation.

Q. Okay. And you just mentioned two websites on autism and OCD, correct?

A. I mentioned websites on the autism and OCD spectrum program.

Q. Okay. What would you consider your main website, Dr. Hollander?

MR. DOVEL: Objection. Form.

THE WITNESS: Well, I guess we have those two different websites. There's a research-related website, and there's a clinical website.

QUESTIONS BY MR. MURDICA:

Q. Do you hold yourself out as a researcher in attention-deficit/hyperactivity disorder?

A. Well, I -- I'm an expert in impulse control disorders and impulsivity,

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and that the ADHD and the mechanisms involved in ADHD are fundamental for impulsivity, impulse control disorders and aggression.

Q. Is impulse control a diagnostic criteria of ADHD?

A. Well, yes, it's one of the domains within ADHD. So there's the inattention domain. There's the hyperactivity impulsivity domain, yes. So, yes, the impulsivity is one of the domains of ADHD.

Q. Okay. So back to my original question.

You, Dr. Hollander, hold yourself out to the world as an expert in ADHD, correct?

MR. DOVEL: Objection. Form.

THE WITNESS: Yes, I'm an expert in ADHD and in neurodevelopmental disorders.

I treat, you know, a large number of children, adolescents and adults with ADHD.

I've gotten grants, federal and nonfederal grants, on impulsivity,

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which is fundamentally related to ADHD.

QUESTIONS BY MR. MURDICA:

Q. Your prior testimony in litigation for plaintiffs has been in litigation over impulsivity like compulsive gambling, correct?

A. Yes, I have offered opinions and testimony around pathological gambling and other impulse control disorders.

Q. Right.

And if we looked -- if we looked at all your prior testimony, we wouldn't see any on ADHD, correct?

A. You know, again, there's a -- there's a -- so impulsivity is one of the domains within ADHD, and ADHD is fundamentally related to impulse control disorders.

Q. So have you held yourself out to another court before this one as an expert in ADHD?

A. Well, I've held myself out as an expert in impulsivity and in impulse control disorders associated with ADHD.

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Q. So any symptom of ADHD you're considering is your expertise in ADHD? That's how you get there?

A. Maybe you could repeat the question --

Q. Sure.

A. -- because I don't quite --

Q. You're saying that -- we'll take, for example, Abilify. You testified about compulsive gambling, right?

A. I testified about compulsive gambling and other impulse control disorders as well.

Q. You did not -- we can look at the transcript. We'd never see the words "ADHD," right?

A. I don't think that that's accurate because I do think that I -- in discussing impulse control disorders, I would have mentioned also the association with ADHD.

Q. To the best of your recollection, did you render opinions in Abilify or Mirapex regarding attention-deficit/hyperactivity disorder?

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A. No. In Abilify and Mirapex, I rendered opinions with regards to impulsivity.
Q. Okay. And the grants that you've gotten for obsessive control disorder, if we looked at the grants themselves, they weren't grants for ADHD specifically, correct? They were for OCD?
A. I've also had grants for impulse control disorders such as pathological gambling.
So I would say that I have made important contributions as it relates to both compulsivity and impulsivity, and I would say that I'm an expert as it relates to both compulsivity and impulsivity.
Q. Okay. Do you remember my question?
A. Well, it had to do with ADHD.
Q. Yes.
A. Perhaps you could read the last question again.
Q. Sure.
The grants you've gotten for obsessive -- OCD, if we look at the grants

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themselves, they weren't grants for ADHD specifically, correct?
A. Well, the grants for obsessive compulsive disorder weren't for ADHD, and the grants for impulse control disorders weren't for ADHD.
Q. Okay.
A. They were for compulsive disorders or impulsive disorders.
(Hollander Exhibit 52 marked for identification.)
QUESTIONS BY MR. MURDICA:
Q. All right. Let's mark your -- I saw -- the questions I was asking you earlier, you had your rebuttal report in front of you. We're going to mark it. We're going to mark a copy. You can use whichever copy you want.
A. I'm fine with my copy.
Q. Okay. We'll just take it here.
Okay. Dr. Hollander, you have in front of you what's been marked as Exhibit 52, which is your rebuttal report.
Do you recognize that?
A. Yes, I do.

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Q. Now, the version you're using is a version you brought with you that has your notes on it, right?
A. Yes, that has my underlines on it.
Q. Okay. All right. So one of the things you do in here in conducting your Bradford Hill is you reference Dr. Baccarelli several times as your reliance for this analysis, right?
A. That's correct.
Q. Okay. When did you first see Dr. Baccarelli's report?
A. I believe I reviewed his report prior to my discussion with him.
Q. And when was your discussion with him?
A. My discussion with him was prior to issuing my initial amended report.
Q. And by that you mean your first substantive report?
A. That's correct.
Q. Okay. And in relying on Dr. Baccarelli, are you deferring to Dr. Baccarelli, or are you saying this is an

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analysis that you, Dr. Hollander, are presenting to stand on its own?
MR. DOVEL: Objection. Form.
THE WITNESS: Well, I've reviewed his report in detail. I agree with the conclusions of his report, I utilize his report as background in preparing my report, and then I offer my opinions in my report.
QUESTIONS BY MR. MURDICA:
Q. All right. So, Dr. Hollander, you don't need Dr. Baccarelli's report to render the opinions in Exhibit 52, correct?
MR. DOVEL: Objection. Form.
THE WITNESS: Well, I'm -- Dr. Baccarelli did a comprehensive review of all of the available literature. He did a comprehensive weighting of each of the different articles and then used the specific methodology, including his navigation guide.
I reviewed, you know, his writing, and I reviewed his use of the navigation guide. I concur with the

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work that he's done, and I rely on the information in his report to support my opinions that are offered in my report.

QUESTIONS BY MR. MURDICA:

Q. Dr. Hollander, are you relying on Dr. Baccarelli's conclusions to support your opinion here?

A. I'm relying on Dr. Baccarelli's report, and I'm relying on his weighting of each of the individual studies. That's in concordance -- so that is supportive of my opinions that are offered in my report.

Q. So if Dr. Baccarelli's got it wrong, then you relied on him, and your report would not be accurate, correct?

A. No, I wouldn't agree with that, because I did my own independent Bradford Hill analysis, which is the standard method to weight the information, you know, in order to render my opinion.

Q. Okay. So this is what I'm trying to get straight, Dr. Hollander.

Do you need Dr. Baccarelli to offer your opinions to the Court here or not?

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MR. DOVEL: Objection. Form.

THE WITNESS: No. I relied on the information in the methods in Dr. Baccarelli's report, but that my report stands on its own in that I conducted my own Bradford Hill analysis of causation, and I offer my own opinion.

QUESTIONS BY MR. MURDICA:

Q. Okay. So while you mentioned Dr. Baccarelli several times here, these opinions in here are yours, correct?

A. That's correct.

Q. Okay. Okay. If we turn to page 8.

Do you recall before lunch I was asking you about temporality?

A. Yes.

Q. And do you see on page 8 you have your temporality section, and you say you "ascribe great weight to the element of temporality"?

Are you on page 8?

A. Let's see. I'm looking at a section that I have on temporality here.

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Q. Yep.

If you turn to page 8 on the bottom.

A. Yeah.

Q. Do you see you have a part F, temporality?

A. Yeah.

Q. Okay. Do you see --

A. Oh, yes.

Q. -- "I ascribe great weight to the element of temporality"?

A. Yes, I see it.

Q. Okay. And this is what we talked about before. It's really a yes or no whether the exposure came before the outcome, right?

A. Yes.

Q. So why did you ascribe it great weight?

A. Well, because if the exposure causes the outcome, then the exposure needs to precede the outcome.

Q. Right.

And isn't that a yes or no question --

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A. Yeah.

Q. -- whether the exposure precedes the outcome?

A. Yes.

Q. Okay. So why would you give a yes or no great weight?

A. Because it would be hard to meet causation under a Bradford Hill analysis if the exposure did not precede the outcome.

Q. Okay. So on the next page, on experiment, you ascribe lesser weight to experiment, correct?

A. That's right.

Q. That was not a yes or no question, right?

A. Well, you know, as I mention here, it's harder to ethically conduct randomized experiments in humans with regard to, you know, prenatal acetaminophen exposure, and so you need to look to other areas such as animal models as well.

Q. Right.

But there is human data on acetaminophen exposure during pregnancy, right?

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A. Well, yes. There's epidemiology data.
Q. Okay. So your justification for ascribing lesser weight here is essentially that there isn't randomized clinical trials?
A. Right. For ethical reasons, it would be impossible, really, to do those kind of randomized clinical trials, for example, comparing exposure to acetaminophen versus exposure to ibuprofen, for example, in pregnant women, and then follow them up and look at the relationship between exposure and outcome --
Q. You --
A. -- because of ethical issues.
Q. You know, don't you, Dr. Hollander, that there are prospective, double-blinded pregnancy registries, right, for this reason?
A. Yes.
Although getting back to your earlier question about EB05, for example, it's more challenging when there's a long time lag, and it's more challenging when

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medicines aren't prescription but over the counter in terms of being able to get that kind of data.
Q. Well, if it's a prospective pregnancy registry that's blinded, it's administered by researchers, so they have that data, correct?
A. Well, I mean, that's the whole point of cohort studies, right? You want to collect that data prospectively with regards to exposure, and then you want to follow up the individuals, and then you want to figure out what the hazard ratios are to determine the relationship between exposure and outcome.
Q. Right.
And those aren't double-blinded, correct?
A. They're not, you know, randomized, controlled trials contrasting acetaminophen to ibuprofen, for example.
Q. Wasn't my question.
They're not -- those registries that you're talking about are not double-blind, correct?

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You know what double-blind means?
A. I do know what double-blind means.
The information is collected prospectively during pregnancy, and the outcome measures are collected independent of those measures. But I guess the subjects are aware of whether or not -- you know, so they're not taking a blinded -- they're not taking a blinded medication. And it's true, you're right. I mean, that's the issue about randomized, controlled trials. You can't give people either acetaminophen or, let's say, placebo to deal with their pain or their fever and then follow them up. That would be a blinded kind of a trial.
Q. Right.
And you've done those before, right?
A. I haven't done them with regards to maternal exposure, but I do them all the time in terms of looking at efficacy and safety with different medications.
Q. For example, treating autism

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with marijuana, right?
A. I have not conducted an autism trial with marijuana. That would be an incorrect statement.
Q. Okay. Are you sure?
A. Yes. I've conducted a trial with compounds derived from the cannabis plant, which is cannabidivarin, which is not marijuana. It's not medical marijuana, no. It's extracting a compound from the plant and doing a randomized, controlled trial.
Q. You've supervised trials trying to -- attempting to treat autism with a marijuana derivative, correct?
A. I am involved in a number of different trials that look at different components that affect both the endocannabinoid system and the phytocannabinoid system. I have not conducted a trial with medical marijuana.
I have conducted a placebo-controlled trial with cannabidivarin, and I'm conducting another placebo-controlled trial with a different compound. And I will be conducting another placebo-controlled

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trial with a FAAH inhibitor that affects the endocannabinoid system, but I have not conducted a trial with medical marijuana.

Q. Okay. Dr. Hollander, with respect to strength of association, you view the strength of a perceived association not by the magnitude but by the statistical significance, correct?

A. No.

Q. Okay. Why not?

A. Because there are different factors to contin -- to sort of evaluate and to consider in terms of looking at strength of association. Statistical significance may be one factor but certainly not the only factor.

Q. Turn to page 8, please.

A. Okay.

Q. You see "Strength of Association," part E?

A. Yes.

Q. Okay.

A. Right.

Q. Third sentence down. "I view the strength of perceived association not by

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magnitude but by statistical significance in determining causality."

Do you see those words?

A. Yes.

Q. You typed those, right?

A. That's correct.

Q. Okay. You just disagreed -- you're arguing with yourself now?

A. I'm not arguing with myself, and I -- so I'm stating that effect size or odds ratio in and of itself, so magnitude of the effect, is not the only factor in considering strength of association.

So even if the magnitude of odds ratio or a relative risk is moderate, if it reaches statistical significance or if it's repeated over and over and over again, then it would be a -- demonstrate a strong association.

Q. Did I read the words on the page in your report on page 8, Exhibit 52, correctly?

A. Well, I believe you read the words on the page. "I view the strength of a perceived association not by magnitude but by

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statistical significance in determining causality."

That's correct.

Q. Okay.

A. However, that's not the only factor. So statistical significance may be one factor, but as we've discussed previously, consistency, confidence intervals, replication, may be other factors.

But this is -- this is correct, this sentence, as you read it.

Q. Okay. And so when you answered that you disagreed with that sentence beforehand, you take that back, correct?

MR. DOVEL: Objection. Form.

THE WITNESS: I would say that it depends on -- it depends.

QUESTIONS BY MR. MURDICA:

Q. Okay.

A. So, yes, statistical significance may be more important than magnitude, but statistical significance is not the whole story. That's my answer.

Q. Okay. On page 11 you say, "Ultimately" -- are you on page 11?

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A. I'm on page 11, yeah.

Q. First paragraph, last sentence. I want to make sure you wrote this.

"Ultimately, I did not have sufficient time to complete a written analysis of each of the studies in sufficient detail."

Did I read that correctly?

A. You read it correctly.

Q. Okay. Now, Dr. Hollander, why didn't you have time to read the studies?

MR. DOVEL: Objection to form.

THE WITNESS: I did have time to read the studies.

QUESTIONS BY MR. MURDICA:

Q. Okay. Why didn't you have time to complete a written analysis of the studies?

A. I had time to read the studies, to process the information, to understand the information in detail.

What I didn't have time to do is an approach such as Dr. Baccarelli did with a navigation guide where he weighted each of the different studies on a number of

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different criteria. That I -- that I did not have time to do.

Q. Dr. Hollander, you were first retained by the plaintiffs' lawyers here months ago, correct?

A. I think it was around February 23rd.

Q. Right.

So you didn't have time between February and July to complete a written analysis of the studies?

A. I had time to read all of the studies. I had time to process the information of all of the studies. I did not have time to weight each study on a number of different metrics. And in that case, I relied on Dr. Baccarelli's navigation guide to do that.

Q. Okay. Have you, Dr. Hollander, ever used the navigation guide in any of your publications?

A. No.

Q. Had you ever heard of the navigation guide before you read Dr. Baccarelli's report?

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A. I have heard of it before. I've never utilized it on my own.

Q. Have you ever read a study prior to being involved in this litigation that utilized a navigation guide?

A. In my practice, I frequently conduct a weight of the evidence, and so I do similar kinds of methods in order to, you know, ascribe different kinds of numerical factors to different weight of the evidence.

So, for example, in the practice guidelines that I've been involved in, we do a very similar analysis. We do a pyramid or a hierarchy where we look at the different studies and different approaches. Then we weight each of those approaches in a different way, and then we utilize that information in order to recommend treatments of different conditions.

Q. Do you remember my question?

A. Well, I think your question is -- one is, did I ever use the navigation guide, and my answer was no.

But I have conducted an approach which is similar, weighting

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different studies on different variables, and integrating that into my practice. So the answer is yes.

Q. Okay. So that wasn't my question.

A. Okay.

Q. My question was, prior to being involved in this litigation, have you ever read a publication that utilized the navigation guide?

A. I -- you know, I don't recall whether or not I -- you know, I'm familiar with the term. I may have read a publication, but I don't recall that publication.

Q. Okay.

A. I haven't utilized that specific navigation guide myself.

Q. Okay. Do you know when the navigation guide was first created?

A. No.

Q. Do you know if it was created 30 years ago? 50 years ago? Five years ago? Any idea?

A. I don't know.

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Q. Okay. Also on this page. "Accordingly, I have relied upon the analysis and assessment of the epi in Dr. Baccarelli's report."

Did I read that correctly?

A. Yes.

Q. Okay. So before I asked you if you are rendering a causation opinion here based on the epidemiology separate and apart from Dr. Baccarelli. But you say here that you're relying on his analysis and overall assessment.

Correct?

MR. DOVEL: Objection. Form.

THE WITNESS: Well, I mean, I think these sentences sort of describe this. So I reviewed the existing scientific research. I didn't have time to do a specific navigation guide analysis on each of the articles. I rely upon his analysis and overall assessment using that guide to weight each of the different articles.

QUESTIONS BY MR. MURDICA:

Q. Dr. Hollander, you didn't do

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your own weighting of the articles; you're relying on Dr. Baccarelli for that, correct?

A. I didn't include a weighting of each of the different articles. I did include a Bradford Hill analysis, which incorporates the data from the analysis, to inform and to guide the opinions that I offer.

Q. So is your testimony here today that you weighted the individual epidemiology studies as part of your Bradford Hill analysis, or you relied on Dr. Baccarelli's weighting in doing your Bradford Hill analysis?

A. Well, I'm relying upon his navigation ratings of the epidemiology, but I'm conducting my own Bradford Hill analysis utilizing the information.

Q. Utilizing his ratings, correct?

A. Well, his ratings are one component. His ratings of the articles give you different strength weightings of each individual article, which helps to inform my Bradford Hill analysis.

Q. Okay. So in doing your

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Bradford Hill analysis, you used Dr. Baccarelli's weighting of the articles based on the navigation guide, correct?

A. That's correct. I --

Q. Okay.

A. -- I review and rely on his navigation weighting --

Q. Okay.

A. -- in order for me to do my own Bradford Hill analysis.

Q. Utilizing his data, correct?

A. Using his particular weighting of the data, although I also conduct my own review of the data.

Q. Okay. And the only documentation, the only analysis, that we have regarding the data is what you have in here because you didn't time to do a separate analysis, correct?

And what you testified to today, fair?

MR. DOVEL: Objection. Form.

THE WITNESS: Well, that's true. I didn't do a navigation analysis on each of the articles.

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QUESTIONS BY MR. MURDICA:

Q. Okay. In the next paragraph, you talk about Baker and Ji, right? That's the next sentence?

A. That's correct.

Q. Okay. And you say, "Both biomarkers serve as concrete measure of APAP exposure."

Right?

A. That's correct.

Q. Were you aware that there was an earlier Ji study that also used a biomarker?

A. I believe that I have seen an earlier Ji study.

Q. Do you know what it used as a biomarker?

A. Perhaps you can show me that, and I can take a look at it.

Q. Yeah, we're going to do that. I was just seeing if you -- if you remember.

Do you know what biomarker Ji 2020 uses?

A. Yes.

Q. What's that?

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A. Umbilical cord blood.

Q. And it says it right there on the page, right?

A. That's correct.

Q. Okay. All right. And then if we turn to page 12, you cite to Alemany, right?

A. Yes.

Q. Okay. And you say that Alemany found consistent positive association between prenatal APAP exposure and ADHD and ASD, correct?

A. That's correct.

Q. Okay. And we are going to look at that one in a minute.

On page 13, you have a section titled "JJCI-Produced Documents."

Let me know when you're on page 13. It's at the very bottom.

A. Yes.

Q. Okay. You know that JJCI is the defendant here, right?

A. That's correct.

Q. Okay. And you conclude the paragraph on page 14, "Since these company

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documents do not consist of any new or unknown primary evidence, I did not ascribe any additional weight to them."

Right?

A. Yes, I see that sentence.

Q. Okay. But you wrote that, right?

A. Yes.

Q. Okay. So your intention here was to look at published data, not internal company documents, right?

A. No.

Q. Okay. What company documents did you ask for, and how did you get them?

MR. DOVEL: As phrased, that is going to invade work product. You'll have to have to rephrase that question.

QUESTIONS BY MR. MURDICA:

Q. Dr. Hollander --

A. Yes.

Q. -- did you ask for company documents?

A. Yes.

Q. Okay. And did you ask for an

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index of what was available from the company?

MR. DOVEL: That's going to invade --

MR. MURDICA: Well, I'm not going to ask for the index.

MR. DOVEL: -- work product, and so as a result, you're going to have to rephrase that question.

MR. MURDICA: I'm not going to ask for the index. I'm just asking if he asked for it.

MR. DOVEL: You're asking about communications. Under the federal rules, you're not allowed to do that, so I'll have to ask you to rephrase.

QUESTIONS BY MR. MURDICA:

Q. Dr. Hollander, do you know how many millions of pages of documents the defendants produced in this litigation?

A. No.

Q. Okay. Did you look at every document produced by the defendants in this litigation, to your knowledge?

A. No.

Q. Okay. And you know that,

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right?

Because you've been involved in litigation. You know that millions of documents are produced, right?

A. Well, it --

MR. DOVEL: Objection. Form.

THE WITNESS: If what you're saying is that there are millions of pages of documents, then I wouldn't have been able to review those millions of pages of documents.

QUESTIONS BY MR. MURDICA:

Q. You reviewed what was provided to you, correct?

A. I asked for relevant documents, and I reviewed them.

Q. Okay. So you just said, I want relevant documents, and that's what you -- and you reviewed what you were given?

MR. DOVEL: As phrased, that calls for communications with counsel.

MR. MURDICA: Look, I'm really not trying to get into your communications, but I have to ask questions in this area.

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THE WITNESS: Could you rephrase that question, please?

QUESTIONS BY MR. MURDICA:

Q. Sure.

Your testimony is that you asked for relevant company documents, correct?

MR. DOVEL: That question --

MR. MURDICA: He already testified to it.

MR. DOVEL: Yes, but that was not in response to a question. As a result, I'm going to prohibit you from asking those questions, which you've not only agreed to in the protocol that was modified, you've also -- subject to federal rules, you'll have to rephrase.

MR. MURDICA: Look, I'll try again, but that's not what our agreement was.

QUESTIONS BY MR. MURDICA:

Q. Dr. Hollander, when you were provided -- after you were provided documents, did you ask any follow-up

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questions about additional documents from the company?

MR. DOVEL: Just as phrased, you're asking about questions -- about communications with counsel. You just didn't put the word "counsel" in your question.

It's improper. You're going to have to rephrase.

QUESTIONS BY MR. MURDICA:

Q. Dr. Hollander, how many pages of company documents did you review in preparation of your report and rebuttal report?

A. I don't recall.

Q. Okay. Was it thousands?

A. I don't think it was thousands.

Q. You don't have any recollection?

A. I don't -- I don't think I reviewed thousands of documents.

Q. And in your regular work when you're doing analyses to publish in the scientific literature, do you get discovery from manufacturers involved in exposures

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you're looking at?

A. Well, I would review material relevant to whatever question or hypothesis I'm testing.

Q. That's public, right? Public material, correct?

A. Well, I would say generally if I'm publishing something, the -- well, the material may be public, although obviously there may be data that's not public that I may review as well, as it relates to the hypothesis of the question.

Q. If you're employed by the manufacturer in some sort, right? In some way?

A. Well, that would be one case.

Q. Okay. And here, you said you don't ascribe weight to the company documents, correct?

A. No. It says I did not ascribe any additional weight.

Q. Okay. You identify forest plots, correct? That's what we're talking about in this paragraph?

A. That's correct.

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Q. Okay. And the forest plots were some internal company pictorial where they put point estimates on a chart with confidence intervals, correct?

A. Well, the forest plots are from this Project Cocoon, and it's a visual representation of the confidence intervals with regards to different studies looking at exposure and outcome. So there are different forest plots for different outcomes.

Q. And you can go get that data from the studies themselves, and indeed you looked at the studies themselves, correct?

A. I have looked at the studies themselves.

I think one thing that's very informative, actually, is by looking at the visual representation of the confidence intervals for the different studies all put together, it provides a beautiful overview in terms of the consistency and the direction of the findings across multiple different studies with different outcome measures.

Q. And you could have done that yourself based on the data, correct?

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A. I think it's possible I could have extracted the data from the individual studies and then prepared a visual chart that represents the different confidence intervals and different outcome measures.

I was appreciative of being able to review that material.

Q. All right.

A. It was informative.

Q. There was no data in what you reviewed that was new, that you didn't have from the literature itself, correct?

A. Yes. Each of the -- I guess each of the visual representations of the confidence intervals could have been extracted from the original data.

Q. All right. Now, on the next page you have your strength of association section.

A. Yes.

Q. And in the third sentence you say, "Importantly, the association between APAP and exposure and ASD and ADHD has been found consistently in meta-analyses and systemic reviews," correct?

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A. Systematic reviews.
Q. And systematic reviews.
And the first study you cite is Masarwa 2018, correct?
A. Correct.
Q. And this came up earlier because you volunteered that this is in your book chapter on autism, correct?
A. Correct.
Q. Okay. So let's take a look at Masarwa. You know what, I'm going to mark it in a second. I have a question first.
To your recollection, Masarwa supports your point here that there's an association between APAP exposure and ASD, correct?
A. Well, in this paragraph, as it's describing it, it talks about the association between prenatal APAP exposure and ASD and ADHD outcomes.
Q. Right.
So both of them. Masarwa supports your opinion on causation for both of them, correct?
A. Well, both of them are listed

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in the sentences above the citation.
Q. Right.
These are your words, right?
A. Yes.
Q. Okay. Did you conduct the literature analysis yourself?
A. Yes.
Q. Did you conduct the literature search yourself?
A. Yes.
Q. Okay. How did you do it?
A. I did that by putting in search terms relating to exposure and outcome.
Q. And where did you put the search terms?
A. To searchable databases such as PubMed.
Q. Okay. And you did that after you issued your initial report and before the rebuttal, correct?
A. No.
Q. When did you do the PubMed search?
A. Prior to my initial report.
Q. Okay. And did you save the

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PubMed search?
A. No.
Q. Okay. Do you remember the search terms?
A. I remember -- well, let me see if I specified in any of the written material what the search terms were that I used.
Q. In medical literature, that's usually -- when there's a search, that's usually what the authors do, right? They explain how they searched and what they searched and what terms they used?
A. Right. You specify what the databases are, and you specify what the terms are, right.
I don't see a description of the search terms.
Q. Okay. And sitting here today, you don't remember what your search terms were, right?
A. Well, I can tell you what I would have entered into it, but I don't recall specifically. And I'm not able to find, but I could look for it a little bit more, whether there's a description of the

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search terms.
Q. Okay. If you end up finding it at any point today, let us know.
A. Okay.
(Hollander Exhibit 53 marked for identification.)
QUESTIONS BY MR. MURDICA:
Q. In the meantime, I'm going to mark this as Exhibit 53.
Dr. Hollander, do you now have in front of you what's been marked as Exhibit 53?
A. Yes.
Q. Okay. Do you recognize Exhibit 53 as the 2018 Masarwa study that you brought up earlier this morning and that we just saw in your rebuttal report?
A. Yes.
Q. When is the last time you reviewed this study?
A. I guess prior to my rebuttal report.
Q. Okay. Do you recall, sitting here today, if this study -- if this -- this is a meta-analysis, right?

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A. Yes.
Q. Okay.
A. It's a systematic review meta-analysis and meta-regression analysis of cohort studies.
Q. Sitting here today, do you recall if Masarwa, in 2018, controlled for genetic factors?
A. Let me take a look.
Q. And, Dr. Hollander, I know there's a question pending, but you're -- you grabbed something.
What is that? It doesn't look familiar to me.
A. This is a summary table of the different individual articles that was prepared by Andrea Baccarelli.
Q. So you printed and brought with you today a marked-up copy of Dr. Baccarelli's summary tables of the articles?
A. Yes.
Q. Okay.
A. However, I don't believe that this, as a meta-analysis, is in the summary

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table.
Q. Can you say that again?
A. I don't believe that this, as a meta-analysis, is included in the summary table.
Q. In other words, what you're looking at --
A. Is a summary table of the individual studies as opposed to the meta-analysis that utilizes pooled data from the individual studies.
Q. Okay. So first of all, let's mark that as Exhibit 54.
MR. DOVEL: Well, you can mark the copy, but that's his --
MR. MURDICA: Sure, yeah, we'll get -- we'll make copies of it.
MR. DOVEL: Yeah, that's going to remain with him. We're not actually going to mark that. We can mark the copy.
MR. MURDICA: Okay. We'll make and mark a copy. Yeah, we'll photocopy it.
(Hollander Exhibit 54 marked

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for identification.)
QUESTIONS BY MR. MURDICA:
Q. Okay. Back to Exhibit 53.
So I -- let me go back to my original question. I think I have your answer.
But as far as you know, Dr. Hollander, Masarwa 2018 has not controlled for genetic factors, correct?
A. No, I did not say that.
Q. Oh, I'm sorry. That was my question.
A. Okay.
Q. Did Masarwa control for genetics?
A. Well, let's take a look at this meta-analysis and see what he does.
Well, in the -- in the methods underneath the meta-aggression, they talk about covarying for a whole range of different factors. But I don't believe that they -- this is not a -- well, let's see what they have here.
So they -- you know, they control for age at follow-up, fever, maternal

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age at birth, smoking, socioeconomic, latitude, duration. And they -- you know, they look at them to understand confounders.
Q. Dr. Hollander, would you prefer to go off the record and take some time to review it?
MR. DOVEL: No, we're not going to go off the record.
THE WITNESS: No, I'm almost there. I've been able to review most of it.
Well, they do comment on it.
So first, as I mentioned, one of the strengths of this is that they covary for a long list of factors, and they find that the association remains significant despite covarying for a broad range of factors.
Then they talk about -- they mention this Brandlistuen report: "Increased risk for neurodevelopmental disorders despite using a sib-matched analysis design, which would be expected to minimize the effect of maternal characteristics on the

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observed observation."
So they comment on that.
QUESTIONS BY MR. MURDICA:
Q. And do you agree with that, Dr. Hollander, that a sib-match design was a good -- is a strong design?
A. Well, I would say that it depends.
So it's one approach to try to control for genetic or familial factors. And there is one study that, you know, shows that in attempting to do that, there's still a strong association.
But there are real problems with the sib-pair approach. And, you know, the huge problem with that is that it essentially negates the effects of mediators and moderators. And I'd like to give you a little explanation of that.
Q. You can, Doctor, when your counsel asks you a question. But I was -- let's stick to my original question, which is that -- did this meta-analysis control for genetics?
A. The meta-analysis discusses

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that as a potential issue and then talks about how that has been controlled, and the findings persist in spite of that.
However -- let me just finish here.
MR. MURDICA: I know, Counsel, you said you don't want to go off the record, but I have a number of studies to go through, and it might save everybody time.
THE WITNESS: Well, I don't -- so -- I mean, this meta-analysis does not use a sib-pair approach. There are -- you know, there are problems with a sib-pair approach if there are mediators and moderators. It just wipes that out, so it's an inappropriate approach.
However, they do discuss the potential for genetic factors, and then they review relevant literature relating to that. And they say that in that, the findings persist despite controlling for that.
But that this study itself,

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they don't -- they control for a large number of different factors. And they find even for controlling many of these factors, the findings persist, so...
QUESTIONS BY MR. MURDICA:
Q. Dr. Hollander, did you see anything here in Masarwa that controlled for parental ADHD or ASD?
A. I don't see that they conducted any -- like a stratification analysis, for example, on those particular factors.
Q. Okay. Dr. Hollander, do you see anything in Masarwa 2018 that controlled for paternal age?
A. Actually, let's take a look at that because I do...
Well, they do control for maternal age.
Q. Do you remember my question?
A. Was it paternal age?
Q. Yes.
A. I'm looking at it now, and I'm seeing if they controlled for paternal.
It's a strong study because

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they used many, many different factors in their meta-regression.
Let's see.
No, it looks like they look at maternal age at birth, but I'm not sure that they included paternal age at birth.
Q. Okay. So as far as you could tell, Dr. Hollander, they haven't controlled for paternal age, correct?
A. I don't -- I don't see a listing of paternal age.
Q. Okay.
A. I do see the maternal age.
Q. And the data here is observational only, right?
A. Well, it's an observational study, but it's pooling different studies that have been conducted, including cohort studies, yeah.
Q. Right.
And the underlying data is observational data, correct?
A. Right.
Q. Okay. And notwithstanding, Dr. Hollander, you think this is a strong

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study, correct?
A. It is very strong.
Q. Very strong study.
And all of the things you were reading were intended to eliminate bias and confounding, correct?
A. Yeah. They do a lot of work to try to eliminate bias and confounding, and they get a strong relationship for exposure and outcomes, including, you know, age of the child on follow-up and duration of exposure. So they find a -- the dose-response relationship here.
Q. Notwithstanding the authors warn that there was evidence of heterogeneity between the study estimates of the outcomes, right?
A. Well, there's great heterogeneity with each of the conditions, and there's a range of different outcomes.
However, you know, what's really remarkable about this is -- so they -- look, they have one, two, three, four, five individual studies, right? And then they have an overall relative risk here. And the

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visual is really strong, actually, for the relative risk ratios for the pooled data.
Q. If you turn to the discussion section --
A. Uh-huh.
Q. -- Dr. Hollander.
A. Yeah.
Q. About halfway down it says, "However, results should be interpreted with caution because there was evidence of heterogeneity between study estimates of the outcome."
Do you see that?
A. Can you direct me to the paragraph?
Q. Sure.
Do you see the discussion section?
A. Yeah, I do.
Q. It's on page 1822, halfway down. "However," on the left column.
A. Right.
Q. That was my question before.
Do you agree with that?
A. Well, I guess the issue is also

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that -- so this first study, the Brandlistuen 2013 --
Q. Right.
A. -- is a relatively small study, which is relatively weak. But I would say that all of the other studies show a strong positive association with confidence intervals that don't cross 1.
So the -- you know, with the exception of that study, there's not a lot of heterogeneity. It looks like it's strong data that's been replicated over and over, which just grows when you pool the data together with the bigger sample size.
Q. Dr. Hollander, the Brandlistuen study you just mentioned, that's the one you said earlier was a sib-control, correct?
A. Let me take a look, because that's 2013?
Q. Well, you were reading it from this article, but, sure.
A. Because that --
Q. Let the record reflect that Dr. Hollander is going to Dr. Baccarelli's tables to answer my question.

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A. Okay.
Q. Which will be marked as Exhibit 54.
A. Let me take a look at that, actually, because that's...
So, I mean, if you see it, it's the -- it's the first one. It's 2013, so it's earlier. And let's take a look at what they have to say with regards to heterogeneity later on, because...
So the -- I mean, this study is really a strong study because they control for so many different potential confounders. They do a sensitivity analysis.
Q. Dr. Hollander, I don't mean to interrupt, but are you talking about Masarwa or Brandlistuen?
A. No, I'm talking about Masarwa.
Q. Okay. Earlier you testified that Brandlistuen has a sibling-control design.
A. Uh-huh.
Q. You don't recall that?
A. I do, actually.
Q. Okay.

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A. Yes.
Q. That was my question.
A. Right.
Q. Okay.
A. I do recall that.
Q. And you gave testimony about how there could be a mediator in the sibling-control design. And my question for you is that if there's a mediator in the sibling-control design of an acetaminophen/autism/ADHD study, that would be -- that mediator would be present in whatever studies utilized sibling-control design, correct? For that same exposure and outcome.
A. Well, so, let me see if I can try to interpret this -- the question in hand.
So we're talking about the relationship between exposure and outcome, right? We're talking about some of the problems with a sib-pair approach.
So let's say that acetaminophen, you know, functions as an anandamide reuptake inhibitor, so it enhances

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endogenous endocannabinoid levels in the developing fetal brain. Let's say enhancing those endogenous cannabinoid levels work via the CB1, and also that FAAH, you know, the enzyme that, you know, creates this AM404 out of APAP, that there are genetic variations. Then the effects of APAP would only be recognized in those individuals who have variations of the CB1 receptor and variations in the FAAH receptor. So -- and that's a family or a genetic impact.
If you utilize a sib-pair approach, then you'd take away those mediators of the CB1 and FAAH genetic polymorphisms, then you lose the results.
So the problem there is that there's a true association. But if you do a sib-pair approach, it's impossible to determine that because you've effectively taken away the mediators that mediate that effect.
Q. Right.
And if that is in fact something that happens, that would persist in whatever sib-pair studies there were for --

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because it would be something that persisted regardless of the study population, correct? If they're siblings?
A. Well, that would be a reason why utilizing a sib-pair approach would -- like a -- bias the study towards the null rather than away from the null.
Q. Okay. If you turn to page 1824.
Do you see the strengths and limitations section?
A. Yes.
Q. The second paragraph down, second sentence, please tell me if I've got this right. It says, "Only a limited number of studies were available for analysis, and all of the studies included were observational design. Most of the studies had some risk of bias, and the results indicated significant heterogeneity."
Did I read that correctly?
A. You read that correctly.
Q. Okay. And I -- you agreed that they were observational. And do you agree that they have risk of bias?

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A. Well, every study has a potential risk for bias, and that's why when you design a study and when you analyze the data, you need to control for potential bias.
Q. And you disagree with them here where they say the results indicated significant heterogeneity.
You don't see it, correct?
A. Well, I really don't see much, actually. I see that there's a strong consistency of the findings with these studies, with one exception.
Q. Okay. And two sentences down -- I had asked you about paternal age -- it says, "In addition, ASD diagnosis is known to be strongly related to advancing paternal age."
You agreed with that earlier toady when I asked you, right?
A. That's correct.
Q. Okay. And it says, "However, none of these studies included paternal age as a covariant."
You just testified that that's -- you didn't see it in here, correct?

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A. Well, I've testified that there are -- they've adjusted for multiple confounders, so they should be applauded for that. But it -- including maternal age. But it's true that they didn't covary for paternal age.

Q. Right.

And that's one of the things that you, Dr. Hollander, associate with the outcomes of ASD and ADHD, correct?

A. Well, let's go over that again, because I believe that that would actually bias it towards the null rather than away from the null.

Q. Okay.

A. So it wouldn't provide a -- it would not provide for a differential. It would be a nondifferential.

Q. All right. So in your view, Masarwa's concern about paternal age here is unjustified, correct?

A. No, I think that Masarwa is doing a good time -- a good job, actually.

So when you author an article like this, you always have to consider the

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strengths and the weaknesses of any individual study, and then you want to try to control for any of those potential confounders or bias.

So, for example, if you look at the design of these studies, they collect information about exposure during pregnancy, and then they look at different measures for outcome many years later.

The cohort nature of the studies, for example, control for things like recall bias as an example.

The design of each of the individual studies controls for various types of bias.

Now, what they're doing here is they're pooling the data from the different studies. And in addition to doing that, then they're trying to look at other potential sources that could be confounders or bias.

And then one of the ways to deal with that, in addition to the original designs of the study, is then to, in a statistical fashion, try to control for those potential confounders by covarying for them.

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And they've done that as well.

Q. And you think they've done a great job at that, right?

A. I think they've done an excellent job at that.

Q. Okay.

A. I mean, no study can do endless amounts of covary. And you always have to read these studies with some appropriate level of detail to look at the strengths and the limitations. And then the authors need to discuss the strengths and the limitations.

But discussing the strengths and the limitations don't negate the findings of the study.

Q. Okay. Dr. Hollander, if you can go to the final page where it says, "Implications for policy and practice," I have two more questions for you on this article.

A. Right.

Q. Halfway down, it says -- do you see where it says, "Our results indicate"?

A. Yes.

Q. "Our results indicate a small

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increase in the risks for ADHD and ASD in the offspring of women exposed to acetaminophen during pregnancy."

Did I read that correctly?

A. Correct.

Q. And do you agree that it's small?

A. No. I agree that, you know, if you look at it, they talk about, you know, statistically significant elevated risks that vary depending on the outcome. So they talk about elevated relative risks that reach statistical significance.

I guess we're getting back to that sentence that you read before in terms of the magnitude of the effect versus the statistical significance.

But if you look at one of the points that I was making is -- if you look at these things and the consistency of the findings, they're replicated over and over again, and so they're statistically significant. You have odds ratios that are above 1. And then there -- so they're -- they're replicated as well, you know.

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Q. Okay. The next sentence where I just read, it says, "However, due to the high heterogeneity in the observed association, the potential for exposure and outcome misclassification and the possibility of residual confounding" --
A. Right.
Q. -- et cetera, et cetera, "further investigation evaluating the observed link is warranted."
A. Right.
Q. Do you, Dr. Hollander, agree that at this point -- that Masarwa, in 2018, further investigation evaluating the observed link is warranted?
MR. DOVEL: Objection. Form.
THE WITNESS: Well, I think that the -- so this was published in 2018. They talk about the potential. So, I mean, it's -- so again, you know, there is a -- you want to make sure that you're -- that you -- that you don't have misclassification. There are various ways to prevent that from happening, for example, such as

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prospective design of these studies.
The possibility of residual confounding, yeah, I mean, they did -- they did actually -- so they talk about maternal characteristics. They did covary for maternal age.
It is true that you do want to address these different issues, right? So, for example, maternal characteristics. And this is something that's come up. It is a good idea to take a look and see whether those maternal characteristics are a factor as a cofounder. Are they related to both the exposure and the outcome.
So studies like Lupattelli have tried to address that where they look at the maternal characteristics, and then they try to determine whether or not the association between the exposure and the outcome persists even if you control for those maternal characteristics.

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QUESTIONS BY MR. MURDICA:
Q. And, Dr. Hollander, you see that genetic factors are listed as one possibility for residual confounding, right?
A. That's right.
Q. And you agreed with me earlier that parental ASD and ADHD diagnoses are not controlled for here, correct?
A. I don't believe that it was -- they didn't use that as a -- to covary.
Q. And if the parents have ASD or ADHD, that is a genetic factor, correct?
A. It's a -- well, it's a familial factor.
Q. Sure. Familial factor.
Okay. Do you see the next sentence? "Considering the significant limitations inherent in the available research, we believe care should be taken to avoid overstating the significance of the results of our analysis because this could promote unnecessary anxiety among pregnant women."
A. I see that.
Q. Do you see that?

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Okay. Did I read that correctly?
A. You read it correctly.
Q. And in your practice, you are asked by some of your patients if they should continue their medicine to treat their OCD, autism, and other diagnoses like that, correct? While they're pregnant. During pregnancy.
A. Yes, I do have mothers who ask me questions about whether or not they should take medicines during pregnancy, yeah. And then we do engage in a risk versus benefit discussion.
Q. Right.
And they're asking you about medicines you prescribe, right?
A. They may be asking about medicines that I prescribe, but -- or they may be asking me about other medicines that they could be taking over the counter as well.
Q. But it's to treat -- they're asking you about medicines to treat the symptoms of the conditions that you're

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treating them for, correct?
A. No, not necessarily. I mean, they're asking me about risk in terms of offspring, and they're asking me about risk versus benefit of them taking various kinds of medicines during pregnancy. And they want to engage in a discussion about the accurate risks versus the benefits of taking any of the compounds versus the potential -- the negative outcome of having a child with ASD or ADHD.
Q. Okay. So you're talking about any medications at all, as if you were their obstetrician, right, Doctor?
A. Well, I'm saying that in my practice I have people coming to me all the time, and I engage in a risk versus benefit discussion with regards to different things that they're taking because there may be benefits to the mother, there may be risks to the fetus. And to make an informed decision, I think that the clinicians and the patients and the families need to have accurate and up-to-date information in order to engage in that conversation.

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Q. And I take it, Dr. Hollander, you don't -- you agree that you shouldn't promote unnecessary anxiety among pregnant women by overstating risks, correct?
A. No. I think it's part of the risk versus benefit ratio discussion, that's correct. So you don't want to cause unnecessary risk by freaking out the parents, and you want to be able to engage in an accurate and informative discussion of risks and benefits. But to do that, you need to have accurate information about the -- both the benefits and the risks.
Q. Okay. Doctor --
A. Absolutely.
Q. Dr. Hollander, in the next sentence, do you see that these authors, in 2018, say that a causal link between exposure to acetaminophen and neurodevelopmental disorders --
A. Right.
Q. -- cannot be established at this point? This is in 2018 they're saying this.
Do you see that?

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A. I see that. And they're -- they are engaging in a risk versus benefit kind of analysis where they're saying you don't want to promote unnecessary anxiety; on the other hand, that this is important information, and so additional work should be done to do a causal analysis, yes.
Q. Okay. And do you agree with them that as of this article in 2018, a causal link between exposure to acetaminophen and neurodevelopmental disorders cannot be established?
MR. DOVEL: Mr. Murdica, is that beyond the scope of this phase, do you think, or not? What do you think?
MR. MURDICA: I think it's a causation question.
MR. DOVEL: Is it specific causation or general causation? How would you categorize that?
MR. MURDICA: I would categorize that as how that contributes to his body of knowledge on causation. If he agrees that this

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isn't enough right now.
MR. DOVEL: So we can ask all your witnesses about the same subject.
MR. MURDICA: Sure.
MR. DOVEL: Okay.
THE WITNESS: Well, I'm saying that the authors are being appropriately cautious and conservative. And what they're saying here is that careful inspection of policies -- and I guess they also mean package inserts as well, patient leaflets, because there's unsupervised and widespread use of acetaminophen, and it's claimed to be a safe, nonprescription medication.
However, they're showing a strong and significant association that persists, despite various kinds of ways to measure or to address confounders or sources of -- sources of bias that persist despite all of that.
So it's a signal that's of concern, and that more work needs to

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be done in order to reach a causal analysis.
QUESTIONS BY MR. MURDICA:
Q. And my question for you, Dr. Hollander, is if you agree with that.
A. Well, I would say --
MR. DOVEL: Let me insert an objection.
Objection. Form.
You can respond.
THE WITNESS: So I would say that in my causal analysis, you know, I was able to look at the results of this study along with multiple other meta-analytic and systemic reviews and individual studies. I was also able to review the animal literature.
And then I was able to use a standardized methodology to be able to review all of that to determine a causal relationship. So I agree that they didn't do that here.
What they did is they took a series of individual epidemiology studies, they pooled the data, they

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wanted to see whether it persisted even when they controlled for various kind of factors. It did persist. They recognize that this is sort of widely used, but they're getting a signal, and they're suggesting that people should really do all the work to establish causality in order to be able to change the risk versus benefit discussion and the labeling relating to this product.
QUESTIONS BY MR. MURDICA:
Q. So in your analysis, Dr. Hollander, this study, this Masarwa 2018 study, wasn't enough to make you determine that there's a causal relationship between acetaminophen and ASD and ADHD, correct?
MR. DOVEL: Objection. Form.
THE WITNESS: Well, I'm saying that this is strong evidence. I utilized this in, you know, performing my analysis in causation. So it's one piece of strong evidence. It's not the only evidence.

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QUESTIONS BY MR. MURDICA:
Q. Okay. Dr. Hollander, can you --
MR. DOVEL: If you're going to move to another topic, we should take a break.
MR. MURDICA: Sure.
MR. DOVEL: Let's go off the record.
VIDEOGRAPHER: The time right now is 2:29 p.m. We are off the record.
(Off the record at 2:29 p.m.)
VIDEOGRAPHER: The time right now is 2:40 p.m. We are back on the record.
QUESTIONS BY MR. MURDICA:
Q. Welcome back, Dr. Hollander.
A. Thank you.
Q. Are you ready to proceed?
A. Yes, I am.
Q. Okay. Dr. Hollander, we discussed the concept of heterogeneity in the context of Exhibit 53, the Masarwa 2018 study, and the authors noted heterogeneity.

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You maybe didn't see it that way.
But here's my question. Can you tell us how you defined heterogeneity in the context of a meta-analysis?
A. I guess -- well, heterogeneity means different presentations, different components.
So I guess they look -- they look at these five studies over and over again from different perspective, and they're all cohort studies. You know, they differ in terms of the year that they were conducted and they differ in terms of the outcome.
So, you know, some of these things look at things like hyperactivity. Some of them look at conduct disorder. Some of them look at ASD. Some of them look at ADHD.
I would say that there's heterogeneity with it -- as it relates to the outcome -- the outcome or the domains of interest, and I would say that there's some variation as it relates to the risk ratios as well.
Q. Okay. So your definition in

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the context of Exhibit 52 is that heterogeneity is difference in the outcome. Some studies looked at ADHD; some studies looked at ASD.

Is that -- is that your testimony?

A. Well, there are, you know, a whole range of different kinds of outcomes that are looked at across these different studies. I guess we could take a look and see what's the context or how they use that word "heterogeneity" here.

Q. Well, Doctor, I'm actually asking you. How do you use -- what's your definition of heterogeneity?

A. Heterogeneity --

MR. DOVEL: Let me insert an objection.

Objection. Form.

You can respond.

QUESTIONS BY MR. MURDICA:

Q. Okay.

A. Okay. Well, I would use heterogeneity as a variation in presentation, a variation in outcome or -- so as it relates

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to these neurodevelopmental disorders, there's a lot of heterogeneity in terms of the clinical symptom domains.

Q. Dr. Hollander --

A. Yes.

Q. -- in the context of meta-analyses generally, does heterogeneity describe differences in the studies in terms of the methods of data observation and collection and things like that?

A. Well, I think you have to interpret it within the context that the word is used.

So here they're talking about heterogeneity in terms of the relative risk for neurodevelopmental outcomes, and they also describe that there are differences in terms of the design, the setting, the populations. So then they also talk about the different tools as well.

So I guess you can have heterogeneity as it relates to the results. You can have heterogeneity as it results {sic} to the design of the individual studies. You could have heterogeneity in

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terms of the outcome.

Q. Okay. And since you disagreed with the authors on the heterogeneity, I was just asking what your definition is.

So if that's -- if you just gave us your best answer, that's good enough for me.

A. Well, so let me -- let me put it this way, that if -- so actually, even in the context here, they're referring to heterogeneity in different ways. So they're talking about -- so they're saying all of the studies tended towards increased risk for neurodevelopmental outcomes, but then they're talking about significant heterogeneity, which they say can be explained by differences. And then they, you know -- they talk about things like design, setting, population.

So -- they actually are -- you know, they're not saying that there are -- because they're -- even in this sentence, they are saying all of the studies show increased risk for neurodevelopmental outcomes. So I guess I agree with them in

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that respect, yeah.

Q. Okay. So are you -- are you broadening your definition of heterogeneity compared to how you were answering before our break?

A. Well, I'm -- I'm -- I've looked at the article. I'm trying to understand their use of the term, and I'm seeing that they better define the term "heterogeneity" in the discussion section, and then they talk about it there, yeah.

Q. Dr. Hollander, have you ever conducted a meta-analysis?

A. Well, I read meta-analyses and interpret meta-analyses all the time. I'm not sure that I have conducted a meta-analysis where I've taken a series of published studies and then I've pooled the data and published it as a meta-analysis.

Q. So then would it be fair to assume that you've never tried to analyze a group of studies to determine whether the data was homogeneous or heterogenous, right?

A. No. Because in my reading of the meta-analysis, I would be able to address

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that.
Q. So I want to make sure I got that answer right.
Your testimony is that you have analyzed different published data sets to determine if they're heterogeneous or homogenous?
A. No, I didn't say that.
Q. Okay.
A. I said that I haven't myself conducted meta-analytic studies but that I read and interpret them all the time.
Q. Okay.
Earlier, before our last break, you were talking about giving advice on medication intake to pregnant women, particularly pregnant patients of yours.
Do you recall that?
A. Yes. Either women who were pregnant or women who were considering becoming pregnant.
Q. Okay. And despite not being board certified in obstetrics, you offer your advice on any range of over-the-counter or prescription medication for your patients in

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pregnancy, correct?
A. Well, I engage in a risk versus benefit discussion with regard to prescription and nonprescription medicines --
Q. Right.
A. -- with my patients.
Q. And you've done that with respect to your patients and acetaminophen, correct?
A. I have.
Q. Okay. And you tell your patients now not to take acetaminophen, correct?
A. No. I say that there are risks and benefits of taking any medication during pregnancy.
Q. Okay. Do you tell your patients if -- if you have a patient that's pregnant and has a migraine, do you -- and they say, Dr. Hollander, can I take acetaminophen, what do you say?
A. Well, I did offer an opinion with regards to that in my initial expert report, which is that I would say that for a woman experiencing pain, I would tell them

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that there are potential benefits and potential risks, but for the use of pain, the risks may outweigh the benefits, and that I would limit the amount of medication; that they should take the absolute smallest number of doses for the shortest period of time and to consider other alternatives.
Q. Okay. So for one of your pregnant patients experiencing migraine during pregnancy, you would -- you would say that the risks outweigh the benefits, correct?
A. Well, I would inform her of information with regards to increased risk of neurodevelopmental outcomes, and I would say that the risk -- there's a dose-response relationship, so that increasing dose and increasing duration would further exacerbate those risks.
And then I would examine the potential benefits and then see if the woman could do without, that they would be aware of what the potential risks are, and then consider other strategies as well.
Q. What other strategies are there

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to treat migraine in pregnancy?
A. Well, there are other prescription and nonprescription medicines that can be used for migraine.
Q. What would you recommend over acetaminophen, Doctor?
A. Well, so this is a key issue here in this particular case. I think one of the things that I find concerning was that mothers were counseled that it was unsafe for them to take nonsteroidal anti-inflammatory medicines such as ibuprofen and aspirin because of the peripheral effects of those medicines. And so they were encouraged to take acetaminophen because acetaminophen didn't have those peripheral effects.
The problem is that acetaminophen has central effects, and the central effects were not well-characterized with regards to neurodevelopmental outcome.
So that I would inform them about the potential risks for taking acetaminophen during pregnancy, and also in terms of dose and duration. And I would caution about the use of that in situations

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where it's not essential, and I would consider other alternatives.

When I reviewed the literature with regards to ibuprofen, I was surprised to see, actually, that the literature is ex -- very modest with regards to the potential risks or outcomes with regards to ibuprofen, for example, with regards to kidney and amniotic fluid and trying to balance the risks and the benefits.

I would not encourage my patients to not take nonsteroidal and encourage them to take acetaminophen. I would encourage them not to take acetaminophen unless absolutely necessary. For example, for high fever.

Q. Right.

And do you remember my question, Doctor? It was what, for your pregnant patients with migraine --

A. Yeah.

Q. -- during the pregnancy, what else would you recommend they take other than acetaminophen?

A. And I would go on to Epocrates,

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and then I would look at all of the prescription options. Then I would review the literature, or I would review what category they are, the risks, the benefits for each of those alternatives. And I would also even consider other nonprescription medicines as well.

And I think that it's important to have a -- you know, an absolute and a relative risk versus benefit for the different medicines and classes of medicines in order to engage in that discussion with patients.

Q. So you would see what Hippocrates says, the program, right?

A. Well, I like Epocrates, but --

Q. Epocrates. You would see what Epocrates says?

A. Well, that would be one way to explore the other alternatives.

The other would be to engage in a discussion: Well, all right, so here is the data with ibuprofen, for example. Here are what are the known risks for ibuprofen. Here's the data for acetaminophen. Here are

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the known risks for acetaminophen. Let's have a discussion and see how this applies to you as an individual.

Q. Do you know what Epocrates says about acetaminophen right now?

A. Well, I haven't -- actually, I'm not -- it would be good to take a look at that. You know, as I mentioned before, it's widely assumed by clinicians and patients and their families that acetaminophen is a Category B medicine, but that may not be the case given the labeling, the more recent prescription versions, where it's no longer listed as a Category B.

Q. You said you were going to go to Epocrates. That was your answer, right?

A. I -- no, I said that that might be one way that I would look into other alternatives.

Q. Name one alternative to acetaminophen, other than ibuprofen, for migraine during pregnancy for one of your patients.

A. There are various prescription medicines for migraine, so -- there are a

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number of prescription medicines for migraine, so I would go on -- I would determine the risks and benefits for those prescription medicines for migraine, and then I would weight it, and then I'd have a discussion with the patient.

Q. Topiramate is one prescription medication for migraine, correct?

A. Topiramate is one prescription medicine for migraine.

Q. Would you give your -- would you recommend your patient take topiramate over acetaminophen during pregnancy for migraine?

A. No, I don't think that I would go to topiramate as an alternative.

Q. Okay. It's one of the only medications indicated for migraine, correct?

A. No. There are other medicines that are also indicated for migraine.

Q. Not a ton of them, right?

MR. DOVEL: Objection. Form.

THE WITNESS: There are a number of prescription medicines, and there are traditional medicines that

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are used for prophylaxis against migraine, so there are several alternatives.

QUESTIONS BY MR. MURDICA:

Q. You know -- you know some of the migraine medications are known teratogens, correct?

MR. DOVEL: I'm not getting time to put my objections in here, so if you could just give me a chance so we don't overlap the court reporter.

THE WITNESS: Thank you.

MR. DOVEL: Objection. Form.

QUESTIONS BY MR. MURDICA:

Q. You know that some of the medications specifically indicated for migraine are teratogens, correct?

A. Well, I do know that. I do know, for example, that valproate is a classic medicine that actually has antimigraine effects and that also is a medicine that causes neurodevelopmental disorders.

Q. You said something about pregnancy categories earlier.

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You know, do you not, Dr. Hollander, that pregnancy categories were abolished in 2015?

A. I do know that those are -- well, not active, but I do know that -- and they don't necessarily apply to over-the-counter medicines as well. But I do know that there are warnings with regards to pregnancy and lactation for prescription medicines.

Q. Right.

My question was, you were referencing pregnancy categories. You know those haven't been used since 2015, correct?

A. I know that that was modified, yes.

Q. Do you disagree with anything I just said? Because you didn't give me a clean answer.

A. Well, I mean, I think even before that time they didn't necessarily apply to over-the-counter. So they only applied to prescription medicines.

Q. Okay. Doctor, you know that the American College of Obstetricians and

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Gynecologists recommend during pregnancy that a woman with migraine should, in fact, take acetaminophen. As of today, that's the recommendation, correct?

A. That's a mistake.

Q. Okay. But you know that that's the case, and you just disagree with it, right?

A. I disagree with it, and I believe that that organization will modify those recommendations over time as they incorporate epidemiology and animal model data.

Q. Have you, in your practice, recommended against the ACOG recommendation to any of your patients who were pregnant?

A. I have recommended to my patients who were pregnant or considering getting pregnant that they -- that it was not safe to use acetaminophen and that they would be at increased risk.

So, yes, I've -- I have not adopted their suggestions because I feel that that would be potentially harmful to my patients.

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Q. Okay. Does your practice -- do you have a medical practice with other doctors?

A. Yes.

Q. Okay. Do they know that you're recommending against medical organization guidelines to your patients?

A. So, you know, doctors need to inform themselves of risks and benefits and engage in those kind of discussions with their patients. They want accurate information.

Q. All right.

A. Yeah, so we would turn to available information to have a discussion with our patients, and we would not just adopt a recommendation from an organization, particularly if we disagree with it.

Q. Okay. Right.

And you didn't come to your conclusion about acetaminophen and ASD and ADHD until you were paid by plaintiffs' lawyers to look at it, correct? This is all new?

MR. DOVEL: Objection. Form.

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THE WITNESS: No, that's not correct. So --
QUESTIONS BY MR. MURDICA:
Q. Okay.
A. -- as I mentioned, I -- after evaluating all of the data, including epidemiology data and animal model data, and what -- and performing a Bradford Hill analysis, I formed an opinion with regards to causation.
Q. Right.
A. And then I utilized that opinion in terms of my discussions with my patients.
Q. Right.
And that opinion on causation you just formed when you did Bradford Hill last month, correct?
A. I did that prior to my initial report.
Q. Okay. When did you do that? When did you do the Bradford Hill?
A. Prior to my initial amended report.
Q. Okay. So prior to June

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of 2023?
A. Yes.
Q. Okay. After February of 2023?
A. Yes.
Q. Okay. So between February and June of 2023, you did your Bradford Hill, correct?
A. That's correct.
Q. And that's when you first determined that there was a causal relationship between acetaminophen and ADHD and ASD, correct?
A. That's correct.
Q. Okay. We were talking about Exhibit 52, Masarwa 2018, for quite a while before the last break.
You remember that discussion?
MR. DOVEL: 52 or 53?
MR. MURDICA: 53. Sorry, 53.
MR. DOVEL: Before we go on, do you have his documents? Let's --
MS. JOHNSTON: I do, yeah.
QUESTIONS BY MR. MURDICA:
Q. Are you ready to proceed, Doctor?

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A. Yes, I am.
Q. Okay. If you look back at your amended -- or your rebuttal report on page 15 --
A. Yes.
Q. -- for me.
Okay. This is how we got onto the topic of Masarwa.
You see on page 15, Masarwa is your first listed study where you say association between APAP exposure and ASD and ADHD has been found consistently in meta-analyses and systemic reviews -- systematic reviews, right?
A. Correct.
Q. Okay. Now, I looked through your report, and I don't see any other Masarwas.
Is that right?
A. Well, I can take a look and see if -- you mean --
Q. Well, do you --
A. -- Masarwa in a different year or --
Q. Yeah. Right.

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Do you recall seeing any other -- in all the work that you did to prepare for this, do you recall seeing any other Masarwas?
A. It's possible, but I don't recall.
Q. Okay. So you don't -- because I didn't see it in here.
A. Okay.
Q. You don't know that two years later Masarwa did an analysis on the biases on --
A. Oh, I'm sorry, I do -- you know, I do know it, and I did cite it in my report.
Q. Okay. And what page is that?
A. I cited it on page 24.
Q. Okay. So, Doctor, you know -- on page 24.
Oh, which report are you looking at?
A. The rebuttal report. It's under A, Surveys in Lieu of Clinical Diagnoses.
Q. Your --

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A. And then I'm actually citing the Faraone report at 67.
Q. Okay. Oh, right. You're quoting Faraone?
A. Yeah.
Q. Yeah, that's not -- that's a quotation of Faraone's report.
A. Right.
Q. Okay. So your report -- do you know what Masarwa 2020 says?
A. Well, I can -- know what it says as it relates to Faraone quoting that.
Q. Right.
You didn't go and get it yourself, correct?
A. Well, I'm not sure if I -- well, let's take a look at the materials cited list.
Yeah, I cited both the 2018 study, and I also cited the 2020 study.
Q. That's in your list of reliance materials, correct?
A. That's right.
Q. Right.
Do you recall reading it?

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A. Yeah, I recall seeing it.
Q. You read everything in your reliance list?
A. Yeah, I relied on all this information.
Q. I asked you, did you read everything in the reliance list?
A. I reviewed it. I didn't read every word in every article, but I did review these articles and incorporate them into my opinion.
Q. Okay. So you didn't -- you didn't cite Masarwa 2020 in your opinion; you quoted Dr. Faraone.
But my question is this, regardless, Dr. Hollander, do you recall what Masarwa 2020 determined?
A. Well, I can -- I can tell you what Faraone was quoting from the Masarwa 2020.
Q. Well, Dr. Hollander, you quoted that because you disagree with Dr. Faraone, correct?
A. I do disagree with Dr. Faraone.
Q. Okay. So sitting here today,

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you don't -- you don't know what Masarwa 2020 says, right?
A. Well, the issue at hand is differential versus nondifferential misclassification. So misclassification that affects both cohorts, so in terms of outcome, really doesn't have an effect. So the issue is really whether there's a differential bias or a nondifferential bias.
Q. And did you -- did you do that analysis and make that determination with respect to Masarwa 2020?
A. Well, I can do that with regards to any study.
Q. Right.
And did you do that before you rendered your opinions here?
A. Well, let's take a look at my rebuttal report here.
Q. Let me know what page you're on.
A. I'm on page 24.
Right. Okay.
Q. Okay. So did you do an analysis on Masarwa 2020, and if so, what was

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your conclusion?
A. Well, I did an analysis on all of the available literature with regards to differential and nondifferential misclassification.
Q. And misclassification as to what?
A. So what Dr. Faraone is contending that Masarwa said is that he's suggesting that caregiver-reported questionnaires could -- or even health care provider diagnoses could somehow have a nondifferential misclassification if the provider knows about the parent's use of acetaminophen.
Q. Okay. And you disagree with Dr. Faraone on that, correct?
A. Oh, yeah, I do. I do disagree.
Q. Okay. And is that why Masarwa 2020 is not cited in your statement affirmatively?
A. Well, I did mention that it is in my materials relied upon list.
Q. Right. Sorry, I'm talking -- I'm talking about your rebuttal report. Your

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report.
MR. DOVEL: Objection. Form.
QUESTIONS BY MR. MURDICA:
Q. Dr. Hollander, you didn't --
A. Yes.
Q. You didn't find Masarwa 2020 to be important enough to cite, correct?
And in fact, you disagreed with Dr. Faraone's citation of it?
A. Well, I do disagree, yes.
Q. Okay. I'm going to mark --
A. And I can explain a little bit more about --
Q. Go ahead. Explain it, please.
A. So that, look, these are cohort studies, right? So you have exposures being assessed at one time point. And then you have a prospective study where then individuals go on to develop the disorder, let's say ADHD, over time, right?
The reporting of the diagnosis over time is not influenced by the classification of the exposure, which is systematically assessed for during the pregnancy period, and then there are two

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aspects to the follow-up or outcome measure.
So one aspect could be utilizing valid and reliable scales. Another way to do that would be to examine medical records for diagnostic codes.
Medical records for the diagnostic codes or the well-validated outcome measures that are administered are done without the knowledge of the exposure. So they're not influenced -- so they're independent variable from the exposure variable, both in terms of temporality, because the exposure variable is collected at the time of pregnancy, and the outcome measure is collected over time in this kind of longitudinal kind of follow-up.
And then the other point is that there are various ways to kind of get that outcome measure. The outcome measure can be based on validated scales, or the outcome measures could be based on clinical diagnoses.
But there's -- that's a -- that's a nondifferential classification, because any kind of bias that could happen

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would be independent of the cohort.
Q. Dr. Hollander, do you know that Masarwa 2020 determined that unmeasured confounding caused their results in 2018 and it was not a valid correlation?
A. Well, I know that unmeasured confounding is always a potential concern. So that means that it's possible that some variable that hasn't been considered is influencing the relationship between the exposure and the outcome, right? So there's un -- unknown variable.
There are other ways to deal with that, such as the use of negative controls. So a negative control would take away that as a potential risk because the negative control would be looking at it at the different time points.
So you get the same -- if you get the -- if you get the finding in the pregnancy and follow-up time but you don't get it when these -- when the variable is before or after, then that would suggest that the unmeasured confounder -- confounders aren't influencing the relationship.

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Q. Dr. Hollander, don't you think it's important that when you're rendering a causation opinion that you consider an author's own determination that their meta-analysis was biased?
A. Well, I'd be glad to review that article with you now, but I can tell you that probably the best way to deal with the unmeasured confounders is by using a -- you know, a negative control. That's probably the best way to deal with that.
Q. And do you recall Masarwa using a negative control?
A. I'm not sure that he did, but there are a number of other examples of the use of negative controls which show that the relationship between exposure and outcome persists even after the negative controls.
Q. And I'm -- we're talking about Masarwa, Dr. Hollander.
A. Okay.
(Hollander Exhibit 55 marked for identification.)
QUESTIONS BY MR. MURDICA:
Q. Okay?

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Let's mark this as Exhibit 55.
A. Right.
Q. She needs to put a sticker on there.
Dr. Hollander, you should now have in front of you what's been marked as Exhibit 55.
Do you see it?
A. Yes.
Q. Okay. Do you see that to be by a Reem Masarwa?
A. Yes.
Q. Do you see that it's dated 2020?
A. Yes.
Q. Do you recognize this as the same author of Exhibit 53?
A. Yes. The same author but a different publication.
Q. Okay. And this publication is a bias review of the prior publication, Exhibit 53, correct?
A. Yes, they're examining that specific issue.
Q. They're examining the specific

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findings of Masarwa 2018 for bias, correct?
A. Correct.
Q. Okay. I'd like you to turn to the final page.
And by the way, do you recall reading this before today?
A. I have seen it before.
Q. Okay. So to the extent it's not in your report, that was a choice you made, right?
MR. DOVEL: Objection. Foundation.
THE WITNESS: I mean, again, I see it in -- in my -- it's mentioned in my rebuttal report and in materials considered.
QUESTIONS BY MR. MURDICA:
Q. In your rebuttal report, it's a quotation from Dr. Faraone's report, right?
A. Correct.
Q. Okay. So my question was, to the extent this is not in your report, that you didn't raise it, that was a choice. You reviewed this before you rendered your report, correct?

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MR. DOVEL: Objection. Form.
QUESTIONS BY MR. MURDICA:
Q. Can you answer my question, Doctor?
A. I'm trying to -- well, I'm saying that it is addressed in the rebuttal report.
Q. Okay.
A. In fact, I respond to this in the rebuttal report.
Q. Whatever you included or didn't include in your report was a choice, because your testimony is that you reviewed this before your report, correct?
A. Yes.
Q. Okay. Turn to page 316, conclusions, please.
A. Uh-huh.
Q. First sentence. "The observed association between acetaminophen use during pregnancy and increased risk for ADHD in the offspring is likely the result of bias. This systematic error appears to be predominantly driven by unmeasured confounding and exposure misclassification."

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Did I read that correctly?
A. You read it correctly.
Q. So you, Dr. Hollander, knew that the authors made this conclusion and just testified for an hour about how important and how strong Exhibit 53, Masarwa 2018, is, correct?
MR. DOVEL: Objection. Form.
THE WITNESS: Well, I did mention that the Masarwa study was strong, and I also addressed the issue here of what -- the unmeasured confounders.
QUESTIONS BY MR. MURDICA:
Q. So to -- for Dr. Hollander, Exhibit 55 doesn't change any of the opinions and testimony you offered about Exhibit 53; is that fair?
A. I think it doesn't change my opinions, and the reason for that is that the -- this issue has been addressed by the use of the negative exposures. You can -- you can take that into account by doing that other way to assess it.
Q. Dr. Hollander, I'm asking you

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about Masarwa 2018.
A. Right.
Q. You testified at length about Masarwa 2018 and its importance to your opinions, and my question is this, Dr. Hollander.
A. Right.
Q. You considered what's in front of you, Masarwa 2020, before you offered that testimony, correct?
A. That's right.
Q. Okay. Do you -- you can see that these authors are from Montreal, primarily from McGill University.
Are you familiar with that institution?
A. Yes, I am.
Q. Do you have any reason to criticize the authors or their institution?
A. No. I think that's a strong institution.
Q. Okay. I'm going to mark -- by the way, is the -- are the supplemental materials to Masarwa 2020 listed on your reliance list?

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A. Well, it looks to me like pages 309 to 317 are listed in my materials considered --
Q. Okay.
A. -- list.
Q. So as far as you know, you did not go and look at the supplemental materials for Exhibit 55, correct?
A. I'd be happy to look at them now if you --
Q. Okay. And that's fairly common for studies like this, that the authors, so that they don't clog up the journal space, they provide their data in supplemental tables you can get online, right?
A. Well, there are different reasons to put material -- list supplemental material. You know, one is there are other -- it's material that sort of provides additional evidence from the study but doesn't directly relate to the question, you know, at hand, so it's not critical. There's always an issue in terms of reducing the space of the number of articles. So --
Q. But at --

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A. -- you know, material is put in supplemental material sometimes because it's not part of the specific primary question being tested.
Q. And my only point, Doctor, if you -- would you agree with me that it's fairly common to have supplemental materials --
A. Yeah.
Q. -- for publications?
A. I would agree.
(Hollander Exhibit 56 marked for identification.)
QUESTIONS BY MR. MURDICA:
Q. Okay. Let's mark this as Exhibit 56.
Doctor, you now have in front of you what's been marked as Exhibit 56.
Do you see it?
A. Yes.
Q. Okay. Do you agree that you haven't seen this before today?
A. This comes from the supplemental material from this --
Q. Yeah, my --

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A. -- 20 --
Q. I'm making a representation to you, and if you did the comparison of what's studied, I'm sure you can -- you could agree with me. But my representation to you is this is the supplemental tables for Masarwa 2020.
A. Uh-huh. Let me take a look.
Q. Doctor, the question that was pending is whether you believe you've ever seen this before.
A. I don't know whether I've -- I don't think I've reviewed this in detail.
Q. Okay. I'd like to direct you to the fourth page.
Do you see E-Figure 2, Doctor?
A. E Table 2?
Q. E-Figure 2. Go one more. Go one or two more pages. One more page from there. Right in front of you. E-Figure 2.
A. Okay.
Q. It's titled "Unadjusted Advised Corrected Risk Ratios for Unmeasured Confounding Parental ADHD."
Do you see that?

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A. Yes.
Q. Okay. So do you see the little chart?
A. Yes.
Q. And we know you like -- we know you like charts because you were talking about the JJCI plots before, right?
A. Well, I do like visual figures that represent the data, yes.
Q. And so you see what happens when Masarwa went and corrected for the parental ADHD, which is a marker of the genetic influence of ADHD, the correlation disappeared.
And you see the -- you see the asterisk way below the dots, unadjusted and biased corrected?
A. Well, I would disagree with one component that you said, again, which is that you said the parental ADHD represents the genetics. So I don't agree with that. That represents the familial, right?
Q. Okay. Doctor, if you match up Exhibit 56 with Exhibit 55, you will see that the parental ADHD influence, when corrected,

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was the bias that caused the results in Masarwa 2018 that you were very excited about.
Do you see that change in E-Figure 2 on Exhibit 56?
A. Well, I see E-Figure 2 in Exhibit 56, and I see that they have the unadjusted. And then what they're trying to do is deal with one unmeasured confound, which is parental ADHD, right? And so they have the unadjusted, and then they have the bias corrected.
And I see that for one, two, three, four, five studies, when you correct it, the risk ratio goes down somewhat. And then I see in two studies it doesn't go down, or it -- or it goes up.
Q. And do you see, Doctor, number 2, the second study? That's Liew, right? That was the very large cohort study. That was what was driving the meta-analysis.
Do you recall that?
MR. DOVEL: Objection. Form.
THE WITNESS: Well, let's take a look and see if that was what was

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driving it. In order to make any statement about that, I need to go back.
Can I have the --
QUESTIONS BY MR. MURDICA:
Q. Sure, Doctor.
A. -- the original?
Q. I thought you had it in front of you.
A. Oh, here we go.
Well, I don't really see that, to tell you the truth. So I'm looking at -- I guess you're referring to Figure 2 because this is the risk ratio for these six cohorts for attention-deficit/hyperactivity disorder, right?
And I'm looking at the Liew article, and I'm looking at -- no, I mean, that's not driving the -- it's right in the middle of the overall. So that's not one of the studies that has the higher relative risk and is driving the overall risk ratio.
Q. Dr. Hollander, is that -- your belief is that what drives a meta-analysis is the risk ratio? And that's what drives a

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study's influence on the meta-analysis, not the number of participants?
A. No, I think -- well, they both can influence it. So it's both --
Q. Right.
A. -- the sample size and the risk ratio.
Q. Right.
And we're going to look at other meta-analyses and --
A. Yeah, but you're -- what you're saying is just not right. If you look at it, the Liew -- so -- all right. So when you --
Q. That's --
A. -- correct for unmeasured confounding, which is parental ADHD in number 2, which is the Liew, and then you look at it here, the Liew study is actually, if anything, pulling the overall risk ratio down rather than driving it up. Because it's somewhat below that.
Q. It's your belief, Dr. Hollander, that each of the risk ratios is considered equally and they're just averaged, right?

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A. No.
Q. Okay.
A. No. I think you're right, and so sample size plays a role.
Q. Okay. Well, you just said I'm wrong, now you're saying I'm right. So you need to pick one.
A. Well, if you look at the -- look at the risk ratio.
MR. DOVEL: Just let me insert an objection.
THE WITNESS: Yeah.
MR. DOVEL: That question -- are you sure you want that question to stand? I mean, it's unintelligible.
You can respond.
QUESTIONS BY MR. MURDICA:
Q. Dr. Hollander, it is not your testimony that a meta-analysis is done by averaging the point estimates of the studies in a meta-analysis, correct?
A. That's correct.
Q. Okay. Because it's a combination influenced by the number -- the N, the number of participants in the study,

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along with the risk -- with the risk ratio that determines the ultimate point estimate in the meta-analysis, correct?
A. That's correct. But if you look at the risk ratio or the point estimate and the confidence intervals, it doesn't matter how -- if anything, if it's larger or smaller, it's actually dragging the risk ratio down rather than pulling it up.
Q. Okay.
A. So it -- but I'm responding to your comment, which it was the -- you said that the Liew study was what was dragging the risk ratio up, and that's just not the case.
Q. I didn't say -- okay, Doctor, I -- the meta-analysis in 2018 determined that it was positive and statistically significant, correct?
Overall, the meta-analysis conclusion found a positive and statistically significant association, correct?
A. Well, that's correct. And also a relationship between, you know, age at follow-up and exposure, yeah.
Q. So, Dr. Hollander, do you not

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understand that if the largest study is attenuated --
A. Uh-huh.
Q. -- by parental ADHD, that could take away, and in fact did take away, the statistical significance of the meta-analysis overall? And the point estimate for that individual study doesn't matter.
MR. DOVEL: Objection. Form.
THE WITNESS: No. Again, I disagree because --
QUESTIONS BY MR. MURDICA:
Q. Okay. If you don't understand it, that's fine.
MR. DOVEL: The witness was responding.
MR. MURDICA: I just want to get it on the record.
MR. DOVEL: You cut him off. I'd appreciate if you let him finish his answer.
THE WITNESS: I think that you were making the statement that the overall risk ratio was biased because of this unmeasured confounder,

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parental ADHD, and it was the Liew study, number 2, that accounted for that.
But I'm telling you based on Figure 2 that the -- if you look at it, the relative risk for the Liew study is only 1.29.
QUESTIONS BY MR. MURDICA:
Q. Okay.
A. Whereas the relative risk for the Streissguth study and the Thompson study and the Stergiakouli study are all well above that.
So I disagree that that's what's -- I disagree that this impact on the Liew study is what is driving the elevated relative risk here.
Q. Okay. And, Doctor, respectfully, we're not talking about the relative risk. We're talking about the statistically significant findings in the meta-analysis.
Do you understand that?
A. Okay. That's a different issue.

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Q. Right. Okay.
So understanding that issue --
A. Okay.
Q. -- do you understand that the Liew study being confounded by parental ADHD could undo the positive finding in the meta-analysis that was statistically significant?
A. I understand that.
Q. Okay. Do you have any basis to disagree between Exhibit 55 and 56 that that's what -- whether you -- that that's what Masarwa determined?
A. Well, first of all, you know, again, I'm getting back to -- even if you're looking at the adjusted versus the uncorrected, the risk ratio is still in the same direction throughout. So it's still a positive relationship, whether it's unadjusted or whether it's bias corrected.
Q. And your testimony on that, Dr. Hollander, you're saying it's still positive, but it's not statistically significant, correct?
A. Yeah, the -- you still have a

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positive association throughout all of the studies.
Q. Okay.
A. The other thing I would say, again, is that there are then other ways to deal with this issue of unmeasured confounders or parental illness.
Q. Do you --
A. So that this is -- I guess this is one way to deal with that.
But I think that what I've said also is that there are other approaches that can deal with these unmeasured confounders where the relationship between exposure and outcome persists.
Q. Okay. And we're still talking about Masarwa. I understand your testimony.
A. Okay.
Q. So let me ask two more questions --
A. Okay.
Q. -- on Masarwa.
A. All right.
Q. Do you disagree with the author's own determination that their 2018

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study was biased, and that's why they found a statistically significant correlation?
A. Well, I do agree that when they adjust for this unmeasured confounder, there -- the risk ratios are lower.
Q. Okay. And the reason you chose not to explain that in your report is what?
A. Because I also talk about other ways to deal with unmeasured confounders for parental effects.
Q. Okay. So it was a choice, that when you cited Masarwa 2018, to not include Masarwa 2020 right after that with a footnote that said, but this effect disappeared when accounting for bias, right?
A. Well --
MR. DOVEL: Objection. Form.
THE WITNESS: I'm not -- I would say that it's -- when you -- when you adjust for it, the findings are less robust but continued to have a positive association.
QUESTIONS BY MR. MURDICA:
Q. Right.
But you didn't put that in your

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report, correct?
A. I didn't put that in my report.
Q. Okay. Let's go to page 15, please, of your amended report. I'm sorry, 12.
All right. Are you on page 12 of your supplemental report, Doctor?
A. My rebuttal --
Q. Sorry, your -- I apologize.
A. -- or my initial report?
Q. Your rebuttal report.
A. Okay.
Q. I led you astray there. My apologies.
A. Okay. Okay.
Q. Okay. Do you remember I asked you some questions about Alemany --
A. Yes.
Q. -- which is listed on page 12?
And then, in fact, if you turn to page 15, which we were just discussing about Masarwa, you'll see that you list Alemany as another consistent meta-analysis along with Masarwa?
A. I see that on page 15, that --

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Q. Yes.
A. -- Alemany is listed along with Masarwa.
Q. Right.
And you relied on Alemany on page 12 as well because it was an exceptionally large group of participants according to you, right?
A. Let's take a look because --
Q. Sure.
A. Well, not only that it was a large group of participants, 73,000 mother-child pairs, but also that it was data from six different European population-based birth cohorts, yeah.
Q. Okay. So we're going to mark this in a second, but when is the last time you looked at the Alemany study?
A. I don't -- well, I don't have a -- I'm not sure. I know that I looked at it prior to preparing my rebuttal, but I can't recall if I looked at it after that time.
Q. Okay. Did you look at these studies in preparation for your testimony

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today? Or was the -- your rebuttal report the last time you looked at them?
A. No. I looked at some of these studies prior to this. I'm not sure that I looked at all of them prior to this.
Q. Okay. We're going to mark this as Exhibit 57.
MR. MURDICA: My colleague tells me we've been going about an hour. This next study is going to take a while.
Do you want to take a five-minute break now?
MR. DOVEL: Yeah, let's take ten minutes?
MR. MURDICA: Okay.
VIDEOGRAPHER: The time is 3:38 p.m. We are off the record.
(Off the record at 3:38 p.m.)
VIDEOGRAPHER: The time right now is 3:54 p.m. We are back on the record.
(Hollander Exhibit 57 marked for identification.)

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QUESTIONS BY MR. MURDICA:
Q. Dr. Hollander, are you ready to proceed?
A. Yes, I am.
Q. Okay. We just marked Exhibit 57, and I'm going to ask you questions about that in a second.
In the middle of the last session, we handed you back the charts that Dr. Baccarelli did on the article summaries, and that now has an exhibit marker on it. And it should say 54 -- well, there's probably a copy that's 54.
Here is my question. Exhibit 54, Dr. Hollander, is really -- it's really two documents, right? One document is a -- or three. One document is ASD studies, one is ADHD, and one is other?
A. That's correct.
Q. Okay. And if you look at the first document, the -- at the -- well, I don't know if it's the first. If you look at the ASD document --
A. Okay.
Q. -- there is, what, five or six

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studies on it?
A. Yes.
Q. Okay. And if you look at the ADHD document, there's more, right?
A. 16, I think.
Q. Okay. Somewhere in the order of 16.
And back to the ASD. Of the -- of the six, one of them is Alemany, which is the meta-analysis, Exhibit 57, that we're about to look at, right?
A. Yes.
Q. Okay. All right. You can put that back aside.
And to your knowledge, I assume you trusted Dr. Baccarelli did a good job identifying the studies that are relevant to acetaminophen and ASD and acetaminophen and ADHD, correct?
A. Yes, he did.
Q. Okay. So you don't have -- you don't have any dispute with the studies that he included on those charts, right?
A. No.
Q. Okay. Back to Exhibit 57.

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This is one of the -- this is the meta-analysis, right?
A. Yes. It's a meta-analysis of six different cohorts.
Q. Okay. And this is -- the outcome here is ASD and ADHD, right?
A. Correct.
Q. All right. And this is Alemany, which you've cited in your report a couple times, right?
A. That's correct.
Q. Okay. And the first sentence of the abstract is that "The potential etiologic role of early acetaminophen exposure on ASD and ADHD is inconclusive."
Correct?
A. That's what the first sentence says.
Q. Okay. And what's the date of this?
A. 2021.
Q. Okay. Do you disagree with that statement that Alemany made for this meta-analysis as of 2021?
MR. DOVEL: Objection. Form.

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THE WITNESS: Well, I believe that prior to 2021 there was lots of both epidemiology evidence and both animal model evidence to inform causation.
QUESTIONS BY MR. MURDICA:
Q. Okay.
A. But I agree with you that that's what the first sentence says.
Q. Right.
So sitting here today, Dr. Hollander, do you know more than these researchers who actually do research on acetaminophen knew in 2021?
MR. DOVEL: Objection. Form.
THE WITNESS: Well, one advantage that I have is I've been able to look at data that included not only epidemiology data but also animal model data. And I don't believe that Alemany, with other authors of epidemiology studies, looked into the animal model data and/or the plausible biological mechanism issues.

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QUESTIONS BY MR. MURDICA:
Q. Okay. And did you contact any of the authors of any of these studies that you're relying on, or that Dr. Baccarelli is relying on, to discuss that?
A. I haven't had conversations with the authors of these studies.
Q. Okay. Have you attempted to reach out to any of them?
A. No, I haven't attempted --
Q. Okay.
A. -- to reach out to the authors of any of these studies.
Q. So whether or not they looked at potential mechanisms or animal data is -- would be complete supposition on your part, correct?
A. Well, I would say that they don't -- they don't discuss it, so they don't -- they do not discuss the epidemiology findings within the context of either the plausible biological mechanisms or animal model data.
Q. You're pretty sure about that?
A. Well, I don't recall seeing

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that. Well, actually, no. Let me -- I'm sorry, let me modify what I said, because even in this article they do -- they do refer to plausible biological mechanisms, including the endocannabinoid system and BDNF and oxidative stress --
Q. So --
A. -- and endocrine disruptors.
Q. So when you just testified that they didn't look at potential mechanisms or animal models, that was not based on fact, correct?
MR. DOVEL: Objection. Form.
THE WITNESS: Well, I would say that these authors did include a discussion of the plausible biological mechanisms within their discussion.
QUESTIONS BY MR. MURDICA:
Q. Right. So back to my original question, which was on the first sentence of the abstract.
Do you, Dr. Hollander, are you sitting here saying you know more than they did in 2021 to gauge the available data to say that they're wrong, that it's

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inconclusive when they write this at this point?
A. Well --
MR. DOVEL: Objection -- let me just get my objection.
Objection. Form.
THE WITNESS: Okay. So, I mean, if you look at the structure of the abstract, they're -- essentially the first sentence is setting up the issue, and then they discuss the aim.
So they're setting up the issue, well, what's the etiologic role? And then to address that, we aim the study.
So I think it's providing a little bit of context and then talking about the aims.
QUESTIONS BY MR. MURDICA:
Q. Right.
A. I don't think that the first sentence is a definitive conclusion.
Q. I agree.
In fact, it says -- Dr. Hollander, it says it's inconclusive,

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correct?
A. Well, even -- I think that their statement about it being inconclusive is not a definitive statement --
Q. Okay.
A. -- because it's introducing the issue.
Q. So sitting here in 2023, Dr. Hollander is interpreting what they could have meant in plain writing in 2021, correct?
MR. DOVEL: Objection. Form.
THE WITNESS: Well, if you look at the last -- so that's the first sentence in the abstract.
And then I would direct you to the last sentence in the abstract, which says, "These results replicate previous work and support providing clear information to pregnant women and their partners about potential long-term risks of acetaminophen use."
So that's their conclusion.
QUESTIONS BY MR. MURDICA:
Q. Right.
Dr. Hollander, I was just

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asking about the first sentence, which says, "The potential etiologic role is inconclusive." That was the first sentence of their abstract.
So when they set out on this, do you doubt that they believed that when they set upon doing this work?
A. Well, I'm suggesting that they're using the initial sentence as an introduction to introduce why would it be valuable to do the study. And then I --
Q. Right.
A. Then what their beliefs are, I think, are captured in the last sentence.
Q. Right.
Doctor, do you have any doubt that when they wrote the first sentence, they didn't mean what they said?
MR. DOVEL: Objection. Form.
THE WITNESS: I don't know whether they meant what they said.
QUESTIONS BY MR. MURDICA:
Q. Okay.
A. I think that they were introducing a reason why this would be a

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valuable study.
I think they were trying to provide some rationale to both the readers and to the editors of the journal on why this article might be of interest.
Q. And when is the last time you reviewed this one?
A. I think I last reviewed this prior to my -- I think prior to my initial expert report.
Q. Okay. So it's been a month and a half since you last looked at it?
A. It's possible.
Q. Did you look at the supplemental materials for this study?
A. I don't recall.
Q. Okay. And you see that this analyzes the cohorts that existed at the time in 2021, right?
A. Yes. And, I mean, it looks like it analyzed these cohorts from, you know, starting -- that were collected between 1991 and 2008.
Q. And one of the things they looked at -- you're familiar with the DNBC,

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right?
A. Yes, I am.
Q. And what does that stand for?
A. It's the Danish National Birth Cohort, I believe.
Q. Right.
And who studied that?
A. Let's see. There have been -- there have been more than one publication resulting from that cohort --
Q. There have.
A. -- so...
Q. All right. So you're looking back at Exhibit 54 --
A. I'm looking at the summary --
Q. -- Dr. Baccarelli's chart?
A. Yeah. I mean, I could get to it, if you like, by going through my report, which tells, you know, which cohorts as well.
Q. Well --
A. But there are -- there's more than one publication that utilized that.
Q. One of --
A. Well, here it is in my report, actually.

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Well, yeah, I talk all about this. I mean, it's one of the world's largest birth cohorts.
Q. Right.
But you've allegedly taken and done an expert analysis here, and you can't tell us who did the studies on the Danish National Birth Cohort?
MR. DOVEL: Objection. Form.
THE WITNESS: Well, I can. I'd be glad to --
QUESTIONS BY MR. MURDICA:
Q. But you don't know it off the top of your head?
A. I can take a look at my report, and I can take a look at my summary tables here.
Q. Okay. The summary tables that Dr. Baccarelli did? Exhibit 54?
A. That he summarized aspects of different studies, yeah.
Q. All right. Don't worry about it. I'll ask you something else.
One of the advantages of the DNBC is that they also can check and see --

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they can look by hospital diagnosis, right?
A. That's correct.
Q. Because with the exception of the DNBC, all of the other cohorts were done by report. Report by the mother or family or something like that, right?
A. Well, that is an advantage of that particular national birth cohort, yeah.
Q. Okay. And did you -- did you look what happened to the effect when they checked the DNBC versus hospital diagnosis instead of just maternal report?
A. Are you referring to the Alemany paper, or are you --
Q. Yeah, I'm talking about Alemany, yeah.
A. Okay. Well, so let's -- if you like, we can examine that.
Q. Yeah, I can help you. It's on page 998.
A. Okay.
Q. Let the record reflect that Dr. Hollander is looking at Dr. Baccarelli's exhibit summary and not Exhibit 57.
MR. DOVEL: That is a false

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statement, and I'd like the examiner to withdraw that statement.
THE WITNESS: Yeah, I'm looking --
MR. MURDICA: Oh, I'm sorry, he's looking at both. I apologize. I thought you were looking at the --
MR. DOVEL: He's not looking at both. I'd still like you to correct your statement.
MR. MURDICA: Okay. Well, I don't know what you were looking at then. You were looking at Exhibit 57 --
MR. DOVEL: If you don't know what he's looking at, don't put it on the record, sir.
MR. MURDICA: Okay. I believe he was looking at Exhibit 54.
THE WITNESS: Well --
MR. MURDICA: They were on top of each other.
THE WITNESS: No, you asked me to examine the Alemany.

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QUESTIONS BY MR. MURDICA:
Q. I am. That's what I'd like you to look at. Page 998 will give you the answer, but you can look at whatever you want to.
A. Okay.
So I'm not sure whether or not your -- well, let's take a look at this one. Hang on a second.
Well, so they examined the results, and they look at this, you know, both with the DNBC and then without the DNBC, without the hospital diagnosis. And they look at, I guess, the odds ratios in boys and girls, with and without that cohort.
Q. Okay. You understand that the first analysis was the DNBC by maternal report, and then it was verified in a second analysis by hospital report, hospital diagnosis, correct?
A. That's correct.
Q. Okay. And when they did the hospital diagnosis, the statistically significant result disappeared, correct?
A. I'm not sure that that's what

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this says here.
Q. Okay. If I could direct you to -- so I think you were talking about something else. We can do that first, Doctor.
Dr. Hollander, when Alemany -- because there's six birth cohorts here, right --
A. No.
Q. -- and DNBC was only one.
When Alemany did an analysis of taking out the DNBC, then it was no longer statistically significant.
That's what you were saying, correct?
A. Well, so they're comparing, like you're saying, so they're getting similar results using the hospital diagnosis. Then they're also looking at it in boys, and they're looking at it in girls. So they're changing this thing around to see if it has any meaningful change.
Q. Right. Okay.
So back to my original question.

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A. Yeah.
Q. You see when they did the hospital diagnosis, the statistical significance of the effect in boys and girls disappeared, correct?
A. Well, I mean, the first statement that they're saying is -- so children exposed to acetaminophen were 19 percent more likely to have ASC symptoms within the borderline or clinical range than nonexposed. So increased odds ratio.
And then they get similar results using the hospital diagnosis.
Q. Okay. And then when they stratify by sex --
A. Right.
Q. -- using the hospital diagnosis, neither sex is statistically significant, correct?
A. Well, no. When they -- so stratifying by sex, prenatal acetaminophen was associated with ASC symptoms among boys, odds ratio of 1.28, with confidence interval of 1.12 to 1.46.
Q. Where are you looking?

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A. I'm looking under the prenatal acetaminophen exposure and ASC symptoms. So this is the first, second, third sentence there on the left side.
Q. Right. Yeah.
A. So there --
Q. And we were talking about hospital diagnosis, Dr. Hollander.
A. Right. And then using the hospital diagnosis, a similar effect was observed where you get an increased odds ratio, 1.14 in boys and 1.15 in girls, although, yeah, it doesn't reach statistical significance there.
But it's --
Q. That was my question.
When using hospital diagnosis, the boys and the girls are -- both are not statistically significant, correct?
A. Yeah, but except you're getting a difference in sample size, right?
Q. Right. Because you're taking -- you're looking at one half and then the other, right?
A. Yeah.

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Q. Okay. And did you -- did you -- were you provided the transcript of Dr. Louie from this past Saturday?
A. No.
Q. Okay. So you don't know what he said at all, right?
A. No.
Q. Do you know who he is?
A. Yes.
Q. Did you talk to him before your testimony today?
A. No, I didn't speak with him.
Q. Okay. Do you agree that a hospital diagnosis is more accurate than a maternal report when looking at the outcome of autism spectrum disorder and ADHD?
A. No. I would say that they are complementary approaches, and that if you get a positive signal using both different approaches, then that's stronger than just doing either one separately.
Q. Okay. So my question for Dr. Hollander is, is hospital diagnosis more accurate and less biased than using maternal report when studying an outcome like autism

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spectrum disorder and ADHD?
A. I would say that there's a high concordance between the two. And so very large-scale studies that have looked at that issue have actually found like a -- concordance rates of up to 98 percent.
So very large genetic studies these days, like the SPARC database, their key is they want to include huge numbers of people in order to really get a handle on these genetic factors. And they don't -- they no longer require like a hospital-based diagnosis, so they go on maternal report.
But then they can look at the concordance rate between the maternal report and the hospital records, and it's very, very high, actually.
So I think they're complementary approaches. I think that basically you get findings in similar directions. That's good. And then that's suggesting different methods getting similar findings.
Yeah, a lot of the statistical significance is -- can be affected by the

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sample size.
Q. Okay. Right. You said a lot there that I didn't ask about --
A. Okay.
Q. -- but let me -- let me ask you another question.
We know the cohort here. We know DNBC is the cohort we're talking about. So you're talking about concordance or discordance among hospital diagnoses versus maternal report in other settings.
I'm talking about this.
A. Right.
Q. DNBC --
A. Right.
Q. -- when you -- when you reduce it to hospital diagnosis, it changes the statistical significance in boys and girls, correct?
A. Well, I think if you read the sentence, it says there's a similar effect, although the level of statistical significance differs.
So there -- you're basically in a similar direction, but --

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Q. But you lose the significance, correct, Doctor?
A. Yeah.
Q. Okay. Now, if you look at A, Table A, right below, do you remember when we were talking before about the Masarwa meta-analysis?
A. Yes.
Q. And we were talking about Liew. And we were talking about the effect that it had, that bias in Liew had, on the overall statistical significance of the Masarwa medical -- meta-analysis.
Do you remember that?
A. I do remember that.
Q. Okay. And you told me that Liew -- originally, before you agreed with me, you said that, well, Liew wasn't a high enough odds ratio and point estimate to change it, right?
And I said, well, don't you have to consider the number -- the population?
So I want you to look at Table A.

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A. Uh-huh.
Q. And do you see that there's a weight given to each study? Each cohort. It's very tiny.
A. A random effects model, right. Yeah.
Q. Right.
Do you see there's a weight column?
A. Yes.
Q. How much weight does the DNBC get?
A. It gets a lot. It gets 47 percent.
Q. It's almost half of the meta-analysis, right?
A. Yeah.
Q. And why is that, Doctor?
A. There's a lot of people there.
Q. How many?
A. It's 61,430.
Q. Out of roughly 70,000, right?
A. Yeah. Well --
Q. Does it refresh your recollection that the DNBC is actually what

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Liew studied?
A. Yeah, let's take a look and then I --
Q. If you have to look at your report to know that, that's fine.
A. No, I recall that, but I'd like to take a look because truthfully there's more than one Liew study, right?
Q. Did they study different populations, Doctor?
A. Let's take a look.
Okay. So you were referring back to the Masarwa article? Here.
Q. Well, I'm really talking about --
A. Yeah.
Q. -- Table A.
A. Okay.
Q. And what's really driving this is the DNBC, correct?
A. Well, that's by far the largest sample size. So you are correct here. Their weighting is high.
And it would go back to the issue with Liew, which was 2014, right? So,

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I mean, you were -- yes, that is the largest sample size, yeah. Okay.
Q. Okay. So you now get the point I was trying to make before with regard to Masarwa, correct?
MR. DOVEL: Objection. Form.
MR. MURDICA: He knows what I'm talking about.
THE WITNESS: Well, I do know that you were reporting that it -- that -- the issue is, yeah, I mean, that study is the largest study, so it has a big impact overall on the meta-analysis because the sample size.
But I -- the point that I was making, A, was with regards to the risk ratio, it didn't pull it up again.
And, you know, with regards to that study also -- well, actually...
QUESTIONS BY MR. MURDICA:
Q. Doctor --
A. Yeah. Okay.
Q. -- because of the effect --
A. Yeah.

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Q. -- that the DNBC has on the data --
A. Yeah.
Q. -- because it's such an important piece, when they pull it out in this analysis, which is right above the table --
A. Yeah.
Q. -- the whole meta-analysis loses its statistical significance, correct?
A. You want to direct me to the figure that doesn't include that?
Q. Yeah, it's literally the very line above that Table A, that teeny tiny writing you were looking at.
A. Oh, the one out analysis.
Q. Yeah.
A. Okay. Well, it doesn't surprise -- so it's saying the association was attenuated but remained positive when -- so that, again, it doesn't surprise me given that 47 percent of the sample size of the weighting comes from that study.
Q. Right. If --
A. But -- okay.

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Q. If the study driving the meta-analysis is pulled out, it can affect the ability to reach statistical significance, correct?
A. Yeah, except that I guess one of the points that I would make here is like here you have a -- in the DNBC, you know, you have a more positive effect on the relative risk here compared to some of the other studies.
Q. You're talking about the 1.19? What are you referring to? What positive effect on the relative risk?
A. You know, if you look at the confidence interval intervals here.
Q. Can you direct me to the one you're talking about?
A. Well, look at A.
Q. A. Oh, ALSPAC? 1.08 --
A. So ALSPAC has a lower confidence interval than the DNBC. The GASP has a -- it's got a broader confidence interval, but the point effect is lower.
Q. In fact, Dr. Hollander, none of these studies, except the DNBC, are actually

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statistically significant with their point effect, correct?
A. Well, it -- I mean, you're right, in this case the DNBC is pulling up the -- rather than pulling it down.
Q. Right. So if you take it out --
A. Yeah.
Q. -- of course it's not going to be statistically significant --
A. Right.
Q. -- since none of the individual studies are, right? Okay.
A. Well, you're going to have a, you know, a lower overall -- so that's what they're saying here, is that the association was attenuated, but it still remains positive even when you take it out. You still have a 12 percent increased risk, but that the -- yeah, the --
Q. But it's not --
A. -- statistical significance goes away.
Q. Okay. All right.

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And, Dr. Hollander, is there any reason that you can think of why acetaminophen should be -- would be causal in boys but not girls in terms of the outcomes of ASD and ADHD?
A. Well, I mean, as you know, like the overall risk in boys is much higher than in girls, right, whether it's 4 to 1 or whether it's 3 or 2 to 1. So there are factors that increase the risk in boys versus girls.
Q. From a teratology perspective, if acetaminophen has anything at all to do with the development of ASD or ADHD in offspring, would it differentially affect boys and girls?
A. It certainly could, yeah.
Q. Why?
A. Well, because gender could be a mediating or moderating factor, right? So there could be some endocrine kind of factors that are moderators or potentially even mediators.
Q. Okay. Have you considered that? Do you have an expert opinion on that?

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A. Well, endocrine factors are listed -- yeah, I do have an opinion. That's one of the plausible mechanisms.
Q. Okay. And so --
A. Acetaminophen might exert its effects.
Q. So in that theory, Dr. Hollander, would there be more -- would more boys or girls have autism or ADHD allegedly caused by acetaminophen?
A. You know, I guess it depends whether or not either endocrine factors or -- could, you know, influence -- you now have all these gene by acetaminophen effects, and you have all of these genetic by acetaminophen effects. It could be that you have gender.
In fact, people look at gender as a covariant -- I mean, in a lot of the studies where they covary for gender, they're not -- you know, the results persist even when you covary for sex. So in many studies, the effects persist despite covarying for gender.
Q. Dr. Hollander, are you offering

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an opinion here today that acetaminophen is sex-selective in terms of the outcome of ASD based on exposure during pregnancy?

A. No, I'm not offering that opinion.

Q. Okay. Are you offering the opinion today that APAP is sex-selective in terms of the outcome of ADHD based on exposure during pregnancy?

A. I'm not offering that opinion now today. I mean, look, if you look at this, they are finding similar findings whether it's boys or girls.

Obviously when you start to look at the differences then -- and they're not -- they're not seeing any statistical evidence of a difference between boys and girls, so they're not doing that. But when you're looking at it in each gender, yeah, then you're lowering the sample size, and that's affecting statistical significance.

Q. Okay. Dr. Hollander, back to the sources of data.

Do you think a study using a screening tool for the outcome based on

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maternal report is better or worse than an outcome measure using a diagnosis?

A. Well, the -- yeah. So the question would be, is there more likely to be a differential bias as a result of using a screening tool as opposed to a differential bias as opposed to using a hospital diagnosis, for example, right?

Because if there's a -- if there's no differential bias, then it doesn't make any difference.

Q. So the answer, Dr. Hollander, is that all things being equal, you would rather have the diagnosis, correct?

A. I think it's good to be able to get similar findings with regards to outcome using different methods. So it's great if you can see similar findings both with a hospital diagnosis and with a screening tool.

Q. If you could only have one or the other, Dr. Hollander, would you rather have a diagnosis or a screening tool maternal report?

A. Well, so that's a challenge, you know, in epidemiology studies, is that

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you want to get a big sample size. It's costly, for example. Sometimes it's a -- costs more to do a study where you're getting a clinician diagnosis as opposed to either an electronic medical record or a scale kind of diagnosis. It's more costly.

But I think one point that I'm making is that it doesn't have a differential effect. So if there's a -- some type of bias introduced using a scale as opposed to a gold standard diagnosis, as long as it's not a differential bias, it wouldn't bias the results towards or away from the null.

Q. Did I ask about costs, Dr. Hollander?

A. Well, cost is a factor in a design -- if you're going to do an epi -- like I say, with cost it -- yes, I -- let me put it that way. If you have unlimited time and unlimited funds, then it's probably a good idea to get clinician diagnoses.

Q. Okay. If you'd turn to the next page and look at Table 4, please.

A. Uh-huh.

Q. Do you see now that the authors

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have stratified the data by sex for both autism and ADHD separately?

A. Yes.

Q. And they've looked at just about an even number of boys and girls for both autism and ADHD. And roughly, each -- boys with autism, girls with autism, boys with ADHD, girls with ADHD, it's roughly 35,000 per group, right? The number of --

A. Yes, approximately.

Q. Okay. And if you look at the boys for autism and ADHD, both of them are statistically significant, correct?

A. Well, it looks like there's a statistically significant finding for the ASC symptoms and the ADHD symptoms.

Q. Okay. And if you look at girls, there is not, correct?

A. Looks like there's a positive association but that it doesn't reach -- well, actually -- but that -- yeah, it looks like it doesn't reach statistical significance there.

Q. Right.

And one of the factors that you

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think about when you do Bradford Hill is an overall concordance, a does this make sense factor, right?
A. Do you mean coherence --
Q. Yes --
A. -- or do you mean --
Q. -- coherence.
A. Okay.
Q. This would not pass the coherence test, correct, Doctor?
Because it doesn't make sense, as you just testified, for there to be a difference between boys and girls.
A. I don't think that I testified that it doesn't make sense for there to be a difference between boys and girls.
Q. Okay. What is your expert opinion about why there's a difference between boys and girls if it's -- that is coherent with the data?
A. Well, one, again, is that -- you know, the obvious reason is that you're -- if you're cutting the sample size in half, then, you know, your power goes down. So that's probably the biggest reason.

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Q. You have no mechanism otherwise to explain why there's a difference. You're saying this is just a statistical anomaly, correct?
A. Well, no. So that's one option, is that you're dealing with a smaller sample size.
I guess I tried to offer an opinion with regards to whether or not there could be, you know, other factors that could mediate or moderate the effect.
Q. Right.
And I asked you if you had an expert opinion sitting here today --
A. Yeah.
Q. -- on what those factors were and the mechanism by which they occur, and you said you do not, correct?
A. Well, no. All I said, that it fits in with this idea of certain hormonal factors, but I wasn't offering a specific opinion.
Q. Okay. Did you look at the supplemental materials related to this study?
A. I don't recall.

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Q. Is it on your reliance list?
A. Let's take a look.
I think that it's hard to determine because I don't see the specific page numbers. So it may not be determinable.
(Hollander Exhibit 58 marked for identification.)
QUESTIONS BY MR. MURDICA:
Q. I'm going to mark the supplemental materials as Exhibit 58.
Dr. Hollander, you should now have in front of you what's been marked as Exhibit 58.
Based on your review -- do you have Exhibit 58 in front of you?
A. Yes, I do.
Q. Based on your review of the first page of Exhibit 58, does this appear to be supplementary material to the Alemany article which is Exhibit 57?
A. Well, it does say supplementary material, and it does relate to the title of the article, and it does include the similar authors, so it does appear that this is the supplementary material to the article.

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Q. Okay. And if you would turn to the fifth page, which says, "Methods S2," and it's a description of the acetaminophen prenatal exposure assessment.
A. Yeah.
Q. Okay. Now, we were just talking, and you saw in the Alemany article there's six birth cohorts, right? And these are the -- and these are a more descriptive version of the six that you saw the acronyms for in the Alemany article.
Fair?
A. Yes. This is a description of each of the different cohorts.
Q. Okay. And one of the features of all the cohorts is that no one asked, and the mothers did not report, the exact day in pregnancy that acetaminophen was used or for exactly how long for each use, correct?
A. Well, if you look at the methods here -- so, for example, in the ALSPAC cohort, the mothers get a questionnaire at 18 and 32 weeks.
Q. Right.
The mothers are getting

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questionnaires, and they're not saying, I used acetaminophen on days 3 through 17 and days 90 through 94 of my pregnancy, correct?

A. Well, it differs a little bit per cohort, right?

Q. Sure.

A. So the first one, you know, again has this questionnaire at 18 and 32.

The DNBC cohort gets a telephone interview at the 12th and the 30th week and postpartum.

And then there are -- there is a list of different medicines. So then...

Q. Doctor, I'd like to you --

A. Each cohort has a -- slightly different methods in terms of exposure.

Q. The way that Alemany counted them, Doctor -- and feel free to take a look at the six descriptions because it's only a page and a half -- is that if acetaminophen was ever used during the pregnancy at any time, it was -- they were counted as users for the purpose of the meta-analysis, correct?

And you can take a minute to

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verify that before you answer.

A. Well, it does say that -- oh, I see. One moment.

Yeah. Well, these were classified as ever-exposed if they reported having taken any dose of acetaminophen in the defined prenatal exposure period. Otherwise they were classified as nonexposed. So, yeah.

Q. Right.

You agree with me that for the purposes of this meta-analysis, Alemany counted them as exposed if they ever took one single pill of acetaminophen at some point during the exposure period, correct?

A. Well, that's what it says in the methods section, yes.

Q. Okay. You don't have any reason to doubt that that's what Alemany did when they wrote this in their supplemental materials, right?

A. No.

Q. Okay. Now, if you look at -- and I think you just did -- the -- with the exception of one, these cohorts all counted

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exposures starting one month before becoming pregnant, correct?

A. No.

Q. Okay.

A. So it says here mothers were asked if they had taken medications from the month before becoming pregnant, in the GASPII and the INMA, or beginning of pregnancy, in the RHEA. So there's a difference depending on the study.

Q. My question was, with the exception of one, these cohorts counted exposures starting one month before becoming pregnant, correct?

Are you looking on page --

A. I'm looking at exposure in the methods section of the manuscript.

Q. Ah. Okay. Well --

A. Because in that, it doesn't say that.

Q. And that's why, when epidemiologists are looking at literature, they look at the supplemental tables, so they can figure out the full methods in the data, right?

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A. Well, it's possible that some information may be included in the supplemental material that's not included in the main manuscript.

Q. All right. Well, why don't we look at the supplemental material and I'll ask my question again.

With the exception of one, these cohorts counted exposures starting one month before becoming pregnant, correct?

A. All right. Let's review that again because that's not what it says in the methods.

Well, no --

Q. Okay.

A. -- I mean, that's not what it says at DNBC. Mothers are classified as users of acetaminophen during pregnancy if they've taken any dose of acetaminophen at any time up during pregnancy.

So it doesn't say anything about taking it prior to -- one month prior. So that's not true with regard to the DNBC.

Q. Okay. Are you sure, Doctor?

A. I'm reading it here from the --

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Q. Supplemental materials?
A. Yeah. Mothers were classified as users of acetaminophen during pregnancy if they had taken any dose of acetaminophen at any time up during pregnancy.
And if you look at the methods also, it doesn't say that with regards to the DNBC cohort. So that's not -- that's not a correct statement with regard to that cohort.
Q. Okay, Doctor.
A. This also --
Q. Look up three -- look three sentences up. Then look at the rest of them.
Did you consider any of this before you rendered your opinions, Dr. Hollander?
MR. DOVEL: Just one second. He was in the middle of answering another question.
Are you going to withdraw the earlier question?
The record is very muddy. I don't know what question is being answered.
I'll state for the record that

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the witness --
MR. MURDICA: Well, what you understand or not doesn't really matter.
MR. DOVEL: Excuse me. Excuse me.
He was in the middle of answering a question --
MR. MURDICA: This is my -- you're interrupting my question. You just be quiet over there.
MR. DOVEL: He was in the middle of answering the question, and then you posed another one before he'd finished. And the record would be fraudulent to suggest otherwise.
MR. MURDICA: You're funny.
QUESTIONS BY MR. MURDICA:
Q. Dr. Hollander --
MR. DOVEL: I try to amuse.
MR. MURDICA: Good job.
QUESTIONS BY MR. MURDICA:
Q. Dr. Hollander --
A. Well, I would say, look, in here there's two inconsistent statements.

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I'm sorry. So there's a statement here, but then it seems to contradict at the end. So --
Q. Dr. Hollander, didn't you --
A. -- I'm seeing a lot of inconsistencies here.
Q. The DNBC is the basis of all the data that you're opining your causation opinion on, right?
A. No.
MR. DOVEL: Objection. Form.
QUESTIONS BY MR. MURDICA:
Q. Do you not know the details around the DNBC and how it was studied?
A. I see that there's contradictory information here, both in terms of methods of the article as well as contradictory statements even within the summary here.
Q. Right.
But didn't --
A. Supplementary material.
Q. But you realize that you're putting these opinions out to the Southern District of New York, a federal court --

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A. Uh-huh.
Q. -- and you didn't even bother to go understand the DNBC?
MR. DOVEL: Objection. Form.
THE WITNESS: Yeah, I think that's an incorrect statement on many different levels.
QUESTIONS BY MR. MURDICA:
Q. Okay.
A. But, yes, A, this is an important study. B, I considered the study in my opinions.
It's not the only study that I included within my opinions, so it's --
Q. The DNBC cohort is a foundational --
A. It's a --
Q. -- cohort for everything you're opining on.
A. It's an important cohort, yes.
Q. Okay. So you know now that the DNBC and all of the others here, except for RHEA, counted exposure starting four weeks before pregnancy or four weeks before conception, correct?

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MR. DOVEL: Objection. Form.
THE WITNESS: I don't see that, actually.
QUESTIONS BY MR. MURDICA:
Q. Okay.
A. And I'm not seeing -- I don't see that in the GASPII cohort either.
Q. Okay.
A. So I think that's -- it doesn't -- that's not right.
Q. Okay.
A. So I disagree.
Q. All right. Well, let's read the second sentence. I'll let you read it.
"Mothers were classified" -- go ahead, you can read it out loud.
A. Okay. "Mothers were classified as users of acetaminophen during pregnancy if they had taken any dose of acetaminophen at any time up to week 32 of pregnancy or the month before becoming pregnant."
All right. You're right. It does say it in that sentence.
Q. Okay.
A. Let's take a look.

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Q. Just let me know when you're satisfied that I'm right about what I tried to start asking you about 15 minutes ago.
A. Okay. Let's take a look.
MR. MURDICA: Let the record reflect that the doctor is looking at Exhibit 57 and not Exhibit 58 right now.
THE WITNESS: Well, I'm reviewing the manuscript that you're referring to to be able to put it into context, what you're putting in front of me in terms of the supplementary material.
Okay.
QUESTIONS BY MR. MURDICA:
Q. Okay. So do you now agree with me that with the exception of the RHEA cohort, all the cohorts counted exposure, if there was exposure, one month before becoming pregnant or conceiving?
A. Well, again, between one month prior to and the end of pregnancy.
Q. Right.
So in -- for the purposes of

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Alemany, if a mother took one pill of acetaminophen 29 days before becoming pregnant, the child was counted as exposed to acetaminophen, correct?
A. Well, not for all of the cohorts, but I guess that's a possibility for some of these.
Q. For ALSPAC, DNBC --
A. Right.
Q. -- GASPII, Generation R and INMA cohort, that was counted as an exposed pregnancy, correct?
A. It's possible that somebody could be classified and fall into that category.
Q. Right.
And did you factor that into your analysis, Dr. Hollander?
A. Well, I would factor it into my analysis because --
Q. Would or wouldn't? I'm sorry.
A. I would.
Q. Okay.
A. Because the dose-response relationship is clear from a number of

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studies, including those studies that used biomarkers.
So, first, with biomarkers, when you're able to assess dosage during the second or third trimester or in studies that look at duration, you have a clearcut exposure response.
So although I guess it's theoretically possible that somebody would be classified, it doesn't -- it's not -- it's not consistent with the idea of a dose-response finding, and it's not consistent with a finding of dosing over time.
Q. And, Dr. Hollander, we're only getting to these one at a time --
A. Yeah.
Q. -- and it seems that as each one, you realize that there's problems you didn't appreciate, you start pointing to the others. And we're going to get to them.
But did you consider in Alemany that an exposure counted even if there was one pill of acetaminophen and even if it wasn't during pregnancy?

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MR. DOVEL: Objection. Form.
THE WITNESS: I guess that gets to the issue of whether or not there could be a misclassification of exposure.
QUESTIONS BY MR. MURDICA:
Q. Okay. And, Doctor --
A. And I guess there are different ways to assess misclassification of exposure.
Q. Right.
And --
A. And I think -- so maybe this Alemany study may not address that potential the same way that some of the other studies do.
Q. Okay. Dr. Hollander, do you know how the symptoms were assessed in Alemany and whether they followed the DSM?
A. Well, it looks like it's a little bit different because they're using terminology such as autism spectrum conditions. So -- and the issue has to do with whether there's misclassification of exposure and/or whether there's misclassification in terms of outcome.

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Q. Okay. Dr. Hollander, if you would turn to Table S2 in Exhibit 58, please.
A. Let's see. What page is that on?
Q. 17. Sorry, I should have given you a page number.
You ready?
A. Yes.
Q. Okay. If you look -- and I'm going to ask you questions about the DNBC.
Do you recall earlier we talked about that they did a -- they did parental questionnaire and then they also looked at medical diagnosis, right?
A. Correct.
Q. Okay. And if you look on the far right for both groups, the children that end up with autism had mothers who had mental health issues during pregnancy at double the rate of the children that were normal, correct?
A. I see that.
Q. Right.
And that -- based on the questions I asked you earlier, you recognize

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depression, maternal mental health, as, I think you said, a factor associated with the outcomes of autism and the outcomes of ADHD, correct?
A. Well, the issue was -- gets to whether or not there's some kind of a genetic confounding.
However, it only has an effect on the relationship between the exposure and the outcome if that results in a behavior that directly influences the exposure.
Q. Dr. Hollander, had you looked at this data and the doubling here in the -- in the population that ended up with autism in terms of maternal mental health?
A. Yes, I'm familiar with that.
Q. Okay. And did you know that that was the case, that there was a doubling in the DNBC?
A. It -- it's essentially the same issue that you had alluded to before with the Masarwa 2020 paper as well --
Q. Okay.
A. -- which is the issue of genetic confounding, right?

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Q. Right. And --
A. And it's the same issue again as -- so if that genetic confounding or that maternal behavior directly affects the exposure, then it's relevant. Otherwise, it's not. Because the -- if you look at the maternal mental health behavior, it certainly could be a mediator or a moderator of the effect of the exposure and the outcome.
Q. Okay.
A. So if you take it away, then you take away the effect.
So, you know, we know that these things are gene-by-environment interactions. This is only an issue if it directly affects the behavior at question, which is the taking of the medicine. And you can -- you wouldn't want to take away the familial or the genetic factors if they directly affect, again, the mediators and moderators.
So the genetic effects affect how the APAP produces the outcome, or it moderates the levels of APAP, then you wouldn't want to be able to take that away.

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In fact, you would need that gene-by-environment interaction in order to get the outcome.

Q. If patients -- if mothers with mental health issues --

A. Right.

Q. -- take acetaminophen more than mothers without mental health issues, it could be mental health, in fact, that's the mediator that attenuates the acetaminophen association you're seeing, correct?

A. Well, it could be that the mental health issues are associated with -- and again, I get back to my example of the cannabinoid-1 receptor or the FAAH. So let's say that women with mental health problems have genetic polymorphisms for the CB1 receptor. They have genetic polymorphisms for FAAH.

If APAP exerts its effects through the endocannabinoid system but there are familial, genetic factors, then it's not a confounder. It's actually a mediator of the effect for the compound. So it's that gene by environment -- you need that in order

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to get the effect.

Q. And, Doctor --

A. And it would still be an effect of the exposure. It would be an effect of the exposure being mediated through that genetic variation.

Q. And, Dr. Hollander, if you're being fair, it could also be vice versa, could it not?

A. How would that be the case?

Q. The way I just explained it.

A. Let me see if I can try to understand that. So --

Q. Have you seen data that women with depression are more likely users of acetaminophen?

A. I have seen publications that talk about behavioral factors as it relates to acetaminophen use.

Q. And --

A. So like the Lupattelli study. So they suggested that, you know, neuroticism or openness, which are two traits in the mothers, you know, could potentially have an effect on APAP usage.

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But the effect was actually really small, and so those individuals interpreted it by saying, look, there's a relationship. It's very small. It wouldn't work as a confounder to wipe out the association, so you can't blame it on the APAP-taking aspect of the mother.

Again, that sort of gets back to the blame-the-mother approach as well, that somehow, you know, these women with mental health problems are more likely to be taking APAP. But it's not an issue if the genetic and familial factors associated with the mental health problems mediate the expression or the effect of APAP on the outcome.

Q. Dr. Hollander, you're blaming the mother as well if you are blaming APAP because the mother took the APAP, right?

Have you considered that when you talk to your patients about causation?

I'll ask another question.

A. Well --

MR. DOVEL: Just a second. He wants to answer.

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THE WITNESS: Well --

MR. MURDICA: Hey, listen, you don't tell me when he wants to answer. He wasn't answering. You don't help.

MR. DOVEL: No, he was answering. He was answering.

MR. MURDICA: Go ahead, Dr. Hollander.

MR. DOVEL: The record will show he was answering.

MR. MURDICA: He wasn't.

THE WITNESS: Actually, you know what I am blaming is I'm --

QUESTIONS BY MR. MURDICA:

Q. The lack of a microphone?

A. I'm blaming the risk versus benefit discussion as it relates to the APAP. So that's what I'm blaming.

Q. Dr. Hollander, are you aware that maternal depression is highly related to increased APAP use?

A. I'm aware that there can be some familial or maternal factors that influence APAP use but that those factors are relatively small. And you'd have to have a

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really big impact in order to wipe out the association between the exposure and the outcome, and that just doesn't happen.

Q. And that's based on what, Doctor?

A. Well, that's based on the Lupattelli study where she addressed that specific question.

Q. Okay.

A. She talked about maternal traits and whether those maternal traits influenced the APAP-taking behavior. And then she related it to different kinds of exposures like SSRIs.

In her analysis of that, she felt that the -- that could be -- play more of a role with certain kinds of exposures and less of a role with other exposures.

Q. Are you familiar --

A. So she determined that that could be a potential confounder as it relates to determining relationship between SSRIs and neurodevelopmental outcomes, but that it wasn't a -- it wasn't a role with regards to APAP use and neurodevelopmental outcomes.

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MR. DOVEL: Time for a break when you get a chance.

QUESTIONS BY MR. MURDICA:

Q. Okay. Have you seen the Bandoli study, Doctor?

A. It doesn't come to my mind immediately --

Q. Okay.

A. -- but I'd be glad to look at that.

MR. MURDICA: Sure, we'll take a break.

VIDEOGRAPHER: The time right now is 5 p.m. We are off the record.

(Off the record at 5:00 p.m.)

VIDEOGRAPHER: The time right now is 5:15 p.m. We're back on the record.

QUESTIONS BY MR. MURDICA:

Q. Welcome back, Dr. Hollander. Are you ready to proceed?

A. Yes, I am. Thanks.

Q. Okay. All right.

Dr. Hollander, are you ready to proceed?

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A. Yes, I am.

Q. Okay. Welcome back.

Dr. Hollander, one of your -- one of the aspects of your opinion is that because ADHD and autism, in your view, share a symptom, that being hyperactivity, that anything that causes hyperactivity is a cause of both autism and ADHD, correct?

A. No.

Q. Okay. Could you please turn to page 32 of your report?

A. This is the original report or the rebuttal report?

Q. Sorry, the rebuttal report.

A. Yeah. Okay.

Q. Okay. On page 32, on the bottom paragraph, it says, "Here, hyperactivity is a symptom domain that is a core feature of ADHD and an associated domain of ASD. If acetaminophen exposure during pregnancy causes hyperactivity in ASD and ADHD individuals, and if hyperactivity is a common feature of ADHD and ASD, then acetaminophen causes ADHD and ASD."

Did I read that correctly?

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A. Yes.

Q. Okay. Do you want to make any corrections to the words in those sentences, or do you stand by those words?

A. Well, I -- maybe I can talk a little about -- so the basic idea is we're looking at symptom domains that present across both neurodevelopmental disorders. I was using hyperactivity as an example of a symptom domain that cuts across both disorders. I wasn't suggesting in any way that it -- that was the key symptom domain that relates the two together.

And in fact, really what I see is that, you know, my work has been in compulsivity and impulsivity, and both conditions share features of compulsivity and impulsivity.

So if I could say it, the compulsivity, both of the disorders have impairment in set shifting, the ability to, you know, let go of stimuli and then refocus on other issues. That set shifting deficit or executive function deficit is like a key feature in terms of the, you know,

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attentional issues in ADHD.
And clearly individuals with ASD also have difficulties in term of set shifting.
The impulsivity, which tightly overlaps with the hyperactivity, is also a feature -- the impulsivity -- the impulsivity/hyperactivity is one domain, and then the impulsivity is a major component as an associated symptom in ASD.
And I would -- and I would relate the compulsivity and impulsivity that I'm describing to the frontostriatal circuitry and the frontolimbic circuitry that's impacted in both disorders.
Q. Do you remember my question?
A. Well, I think your question had to do with whether or not hyperactivity was a symptom domain or feature of both disorders.
Q. No.
My question --
A. Yeah.
Q. -- Doctor, is, do you -- the two sentences that we read together that begins with "here" and ends with the word

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"ASD" on page 32, do you want to correct the words in those two sentences or leave them as-is?
A. Well --
Q. I'm giving you a chance.
A. Right.
And what I'm -- so what I'm suggesting is I might modify hyperactivity to include hyperactivity/impulsivity.
Q. You --
A. As a --
Q. -- don't mean -- Dr. Hollander is not here to tell the Court and the world that anything that has a -- anything that causes hyperactivity causes autism and ADHD, correct? That is not your testimony?
A. Could you repeat that question again?
Q. Sure.
Are you here to tell the world that something associated with hyperactivity means it causes autism and ADHD?
A. No.
Q. Okay. You're not -- you're not saying that if acetaminophen is associated

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with hyperactivity, then it must also cause ASD and ADHD, correct?
A. No, I'm not saying that.
Q. Okay. And impulsivity is not a feature of ADHD, right?
A. Well, it is. The hyperactivity/impulsivity domain, yeah.
Q. Is it a feature of all ADHD?
A. It's a feature of those who have the combined type or the hyperactive type.
Q. Okay. So not every --
A. Not the inattentive type.
Q. Okay. And is hyperactivity a feature of everyone diagnosed with ADHD?
A. No. It's a symptom of those who have the hyperactivity/impulsivity subtype, not just those who just have the inattention subtype.
Q. Okay. If you turn to page 22 of your rebuttal report, please, Doctor.
I want to focus you on the last sentence. Let me know when you're there. I'll read it, and you tell me if I read it correctly.

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Do you see the last sentence that begins "to the contrary"? Page 22 of your rebuttal.
A. Could you read the sentence above that? Because somehow it's not --
Q. Yeah.
It's the paragraph that starts, "In addition" -- that doesn't look right because you have a sub-footnote there.
A. Oh, I see. I gotcha here.
Q. Well -- oh, you have a different version than I do.
A. I don't think so.
Q. I'm looking here. You're on 23. Huh. Go -- oh --
A. "In addition."
Q. Huh. I have to admit, I'm puzzled.
A. Or this "in addition" back here? Baccarelli --
Q. Oh, specificity is -- ah, right here. "To the contrary."
A. Okay. Gotcha. Sorry.
Q. Okay. It does seem -- the pages are not matched up. All right. We'll

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mark that and try to figure it out later. We'll take a copy of it.

Dr. Hollander, you state, "To the contrary, as I have discussed in great detail in my initial report, it is widely accepted that neurodevelopmental disorders, including ASD and ADHD, share important neurogenetic physiological, structural and psychological traits, Barch 2020, period."

Did I read that correctly?

A. Yes.

Q. Okay. Now, is Barch a publication that you're familiar with?

A. Yeah, it's a publication that I've considered in my materials considered list.

Q. Okay. And Barch stands for the proposition that ASD and ADHD share important neurogenetic, et cetera, traits, right?

A. Correct.

(Hollander Exhibits 59 and 60 marked for identification.)

QUESTIONS BY MR. MURDICA:

Q. Okay. Mark Barch -- we're going to mark that report that's different as

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59, and we'll mark Barch as 60.

Okay. Dr. Hollander, you now have in front of you a document that's been marked as Exhibit 60 by author Deanna Barch.

Do you see that?

A. Yes.

Q. Is this what you were referencing in your rebuttal report with the Barch citation?

A. I believe so, yes.

Q. Okay. Dr. Hollander, can you point us to where this article says anything about attention-deficit/hyperactivity disorder or autism spectrum disorder?

A. Well, I mean, this is taking the approach -- again, we're highlighting that symptom domains can be transdiagnostic and can map onto underlying brain circuitry.

Q. We can agree, though, that that article doesn't say ASD or ADHD, correct?

A. Well, it certainly applies to ASD and ADHD. I think in this particular editorial they talk a little bit how these symptom domains cut across things like schizophrenia or bipolar disorder, or they

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talk about bipolar disorder and major depression. So they use different examples.

But the concept is -- can be certainly -- the concept can be applied and is appropriate to the transdiagnostic symptom domains that cut across ASD and ADHD and map onto their underlying brain circuitry and neurogenetic factors.

Q. Dr. Hollander, it doesn't say that. You were citing Barch 2020 as background, not specific to ASD and ADHD, correct?

A. It's talking about a transdiagnostic approach to neuropsychiatric disorders.

Q. Okay. And you can have --

A. Yeah.

Q. Dr. Hollander, you can have symptoms but not have a disorder, correct?

A. Well, yes. I mean, you can have symptoms and symptom domains and not have a disorder.

Q. Right.

You would only be given a disorder in the diagnostic manual if the

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symptoms caused marked distress or interfered with functioning; otherwise they're just symptoms. Right?

A. That's correct.

Q. All right. Now, one of the things that you've mentioned a couple times are biological marker studies, right? And you cite Ji and Baker in your --

A. Baker and Ji, yeah, biomarkers.

Q. Right, biomarkers.

And you think those are important, right?

A. Well, they're a more -- they're a more direct measure of exposure.

Q. Okay. And I noticed you cited Ji 2020, but did you review the earlier Ji study on maternal plasma?

A. Let me see. It's possible that I reviewed more than one of the Ji studies. Let me just...

I think I -- I think if they used similar cohort or approach, that I might have not cited every one of them, yeah.

Q. So which is it? You didn't -- you didn't cite it?

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A. Well, I did cite it.
Q. Oh.
A. I cited the Ji 2020 article.
So are you referring to a different year?
Q. I am.
A. Yeah, which year are you --
Q. 2018.
A. Right. Okay.
Q. Did you cite that?
A. No, because if the 2018 -- I'm sorry. If the 2020 includes a similar cohort, then I would cite the larger or more comprehensive of the studies.
Q. Okay. But with Masarwa, you cited 2018 and not the more current 2020, right?
A. Well, again, the -- so the 20 -- the Masarwa -- the 2018 was the meta-analysis. The 2020 examined one particular issue of bias or confounding but wasn't the original meta-analysis. So --
Q. Okay.
A. -- I cited the meta-analysis, not the article that tested for one

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particular confounder.
Q. And your testimony now is that Ji 2020 encapsulates Ji 2018, so you didn't need to cite it, right?
A. I believe so.
Q. Okay. By the way, the transdiagnostic theory you have on ASD and ADHD is based on the shared feature of hyperactivity, right?
A. No.
Q. Okay. The transdiagnostic theory that you have connecting ADHD and A -- ASD doesn't replace the DSM, correct?
A. It doesn't re -- no, it complements the DSM. So it's -- it's a -- it maps on more closely to the underlying, you know, circuitry or genetic, cellular -- because it -- it's more closely related to the underlying defect, and the diagnosis is more distal to the underlying defect.
Q. Dr. Hollander, is hyperactivity a symptom of anything other than ASD and ADHD?
A. Yes. I mean, hyperactivity can be a symptom. It can be a symptom in other

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conditions.
Q. So your transdiagnosis theory of --
A. And --
Q. Sorry.
A. And it -- and it can -- and it can vary in severity as well. So it's a symptom domain.
Q. Okay. So you agree that hyperactivity is a symptom of much more than just ASD and ADHD, correct?
A. Yeah, as a -- as a -- well, first of all, so the notion of the transdiagnostic is that the domain cuts across different conditions.
Q. Right.
A. That's the sort of definition, and it's not restricted to.
So, for example, I looked at compulsivity like OCD, right? I saw that there were a group of other disorders that shared underlying features. So they had similar clinical symptoms. They had similar familial factors of transmission. They had similar underlying brain circuitry. And as a

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result of that, the DSM was reorganized to include a new chapter called obsessive compulsive and related disorders.
And the reason that that chapter in the DSM was organized was because there was a common transdiagnostic symptom domain that cut across all of the different conditions that are now listed in the DSM-5.
Q. Okay. Dr. Hollander, if acetaminophen causes a symptom domain like hyperactivity, shouldn't it cause, by your logic, every -- not just autism and ADHD, but anything for which hyperactivity is a symptom?
A. Well, again, you know, these conditions are pretty heterogeneous, and they include multiple different symptom domains. Those symptom domains, you know, can cut across different conditions.
There are other symptom domains as well that can co-occur or shape the expression of the disorder.
Q. According to Dr. Hollander --
A. And that -- well, I'm sorry, just let me finish.

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So that APAP, or acetaminophen, can be a causal factor in causing a symptom domain. That doesn't mean, you know, that it's the only factor causing that symptom domain. And clearly there can be other factors or combinations that come together to get the full expression of the condition.

So -- but it -- if APAP exposure affects, through the process of neurodevelopment, a key brain circuitry, and if that brain circuitry regulates that symptom domain, then impacting that brain circuitry would be associated with the development of that symptom domain across other conditions.

However -- but here's the however also. It also depends on like the timing of the exposure and the dose of the exposure, because you may impact -- you may create a -- you may impact or dysregulate a particular circuit at a particular time of exposure or dosage of the exposure but not affect that circuitry with a different type of an exposure.

But that exposure at a

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particular timing that affects the underlying circuitry of development would create those symptoms expressed across different conditions.

Q. Dr. Hollander, is IQ a symptom domain for ASD?

A. No.

Q. Is IQ a symptom domain for ADHD?

A. No.

Q. According to Dr. Hollander, does acetaminophen cause major congenital malformation?

A. No.

Q. According to Dr. Hollander, does acetaminophen cause neural tube defects?

A. Usually no.

Q. Does acetaminophen ever cause neural tube defects, according to Dr. Hollander?

A. No. It causes more subtle kinds of symptoms than major neural tube defects.

Q. Okay. And you -- Dr. Hollander, you just testified that the

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timing is important and the dose is important.

What is the important timing for causation on autism?

A. Well, I mean, the best estimate is exposure during the second and third trimester.

Q. Okay. And when -- according to Dr. Hollander, when is the timing to treat -- to cause ADHD?

A. The second and third trimester.

Q. Okay. So it's the same.

According to Dr. Hollander, what does acetaminophen cause other than ADHD and autism?

A. Well, I mean, it can cause liver failure. So, I mean, it really depends on the dosage and the timing.

Q. Okay.

A. It could cause skin reactions. I mean, it really depends on the dosage and the timing.

Q. Dr. Hollander, when a pregnancy is exposed to acetaminophen in the second and third trimester -- second or third trimester,

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what outcomes in the fetus can acetaminophen cause, according to Dr. Hollander, other than ASD and ADHD?

A. Well, I mean, it can impair circuits such as frontostriatal circuits and frontolimbic circuits that can present with set switching, executive function-type problems and impulsivity/hyperactivity.

Q. And, Dr. Hollander, you have no direct human evidence of that. Your testimony you just -- you just gave is based on animal studies, correct?

A. No.

Q. Okay. What direct human evidence do you have on impairing those exact circuits?

A. Well, the Baker study used functional MRI as a measure of outcome. So they used a direct measure of exposure, meconium, to determine the dose-response relationship, and they used a direct measure of outcome, which is functional MRI. And they determined that there was a relationship between exposure and hyperactivity and hypoactivity of those circuits.

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Q. Dr. Hollander, other than -- how many patients were -- received an MRI in Baker?
A. I'll have to take a look at it to get the exact number.
Q. Was it a lot?
A. Well --
MR. DOVEL: Objection. Form.
THE WITNESS: I -- it would have been a subgroup of the overall amount. So there were 345 subjects overall in the study, and a subgroup of that received a functional MRI.
QUESTIONS BY MR. MURDICA:
Q. Right.
And it's not your testimony that the subjects who had their meconium sampled was direct human evidence of interference with those pathways, right?
A. No. All that was doing was it's a more direct measure of the exposure.
Q. Okay. Other than the MRIs on however many subjects were -- had an MRI measurement in Baker, do you have -- are you relying on any other direct human evidence

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that acetaminophen allegedly interferes with that signaling in the fetus?
A. Well, that -- I mean, it kind of gets to the experiment issue. And there were ethical issues in terms of dosing women with acetaminophen and then doing imaging on the offspring, so that hasn't been conducted.
But I guess animal models would be a good way to be able to do that experiment, actually, and that's what's been done.
Q. And my question was on human data.
The only direct human evidence you're relying on for what we're talking about right now was the subset of Baker that had the MRIs, correct?
A. Well, I am relying on that. That's what comes to my mind now.
I guess I'm also relying on all of the other, you know, outcome measures that were used, whether they were diagnostic outcome measures or scales, and then my understanding of the correlation between those different measures and other

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neuroimaging measures.
So there's a -- there's a lot of information about underlying brain circuitry and these clinical conditions linked to these diagnoses, and there's a lot of information relating to circuits that are involved in the -- you know, cognitive features that are assessed by these outcome measures. So I'm also relying on that literature as well.
Q. Dr. Hollander, on Exhibit 54, which are Dr. Baccarelli's tables that you're relying on, the only -- if you look through them, the only measure that you rely on for direct evidence of circuitry in the brain is the Baker subset, not any of the other studies, correct?
A. Well, I would -- I would have to repeat myself again in that many of these outcome measures that have been tested in these different cohorts have also been studied and correlated with in neurocognitive features and brain circuitry.
However, in the studies that link exposure and outcome directly, yeah, the

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only -- my understanding, the only measure that currently exists in terms of like functional brain circuitry is the Baker study.
Q. And other than ADHD and ASD -- this is how we got on this topic -- what else can acetaminophen cause in the fetus?
A. Well, it can also be associated with other neurodevelopmental problems.
Q. Okay. And have you done an analysis on those? A causal analysis?
A. Yes. I have discussed that, and then I also have relied on Dr. Baccarelli, who has also done a separate navigation weight-of-the-evidence analysis for neurodevelopment, and also has organized that material as it relates to exposure and other neurodevelopmental outcomes.
Q. Is acetaminophen selective at all for neurodevelopmental outcomes, or does it cause all -- all neuro -- all bad neurodevelopmental outcomes, I guess I should say?
A. No, I wouldn't say that it doesn't cause everything as it relates to --

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and as I mentioned again, it doesn't -- so it can affect the liver and it can affect the skin. So it doesn't only affect neurodevelopment, although in the setting of maternal usage, it can be associated with different neurodevelopmental outcomes.

It's not associated with neural tube defects. It's not associated with severe mental retardation.

It is associated with these more subtle symptoms that cut across ASD and ADHD and other neurodevelopmental disorders, and is manifest by executive function set switching problems as well as impulsivity and hyperactivity.

Q. But you go beyond the symptoms, right? You're saying -- Dr. Hollander is here telling the world that acetaminophen causes essentially every adverse neurological outcome in the fetus when the mother is exposed during the second or third trimester of pregnancy, correct?

A. No.

Q. Okay. But for sure, Dr. Hollander is telling the world that

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acetaminophen exposure can cause ADHD and autism in the child, right?

A. Yeah. Exposure to acetaminophen can be a causal factor in the development of ASD and ADHD and other neurodevelopmental disorders.

Q. Okay. And did you see when you looked at Ji, the earlier Ji study, that -- and it was a biomarker. It was maternal plasma.

Did you see that Ji found an association with one of the outcomes but not the other? Do you remember that?

A. I think I recall that, yes.

Q. Okay. And that is not concordant, right?

That does not fit your theory for acetaminophen to cause one of ADHD and autism and not the other, correct?

MR. DOVEL: Objection. Form.

THE WITNESS: I guess I'd have to look at the manuscript in order to be able to offer an opinion --

QUESTIONS BY MR. MURDICA:

Q. Sure.

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A. -- relating to that.

Q. Sure. And I'm going to mark it in a second.

But did you consider discordant results in your analysis between the two outcomes?

A. Yes.

Q. Okay. And to the extent there were discordant results, it didn't impact your conclusion on causation as to both, correct?

MR. DOVEL: Objection. Form.

THE WITNESS: Well, I acknowledged the discordant results. I formed my opinion based on the totality of the evidence.

QUESTIONS BY MR. MURDICA:

Q. Okay. And you've definitely seen Ji 2018 before today, right?

A. I believe so, yes.

(Hollander Exhibit 61 marked for identification.)

QUESTIONS BY MR. MURDICA:

Q. Okay.

A. Well, let me just take a look

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and just make sure that I -- hold on one second in terms of materials considered.

Yeah, that's -- it is included in my materials considered, both the 2018 and the 2020.

Q. You now have in front of you what's been marked as Exhibit 61.

Do you see it?

A. Yes.

Q. Do you recognize that as a study by Yuelong Ji?

A. Yes.

Q. Do you see that it's not the 2020 study that you have cited in your report?

A. Well, I see that it's the 2018 study that's cited in my materials considered.

Q. Right.

This is not the Ji 2020 study, right? They're different.

A. It's a different publication.

Q. This is a maternal biomarker study, though, right?

A. Well, it's part of the Boston

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birth cohort, so it's the same birth cohort.
Q. Do you know the difference between Ji 2018 and Ji 2020?
A. Well, I can tell you that the -- this report is 1,180 children in the Boston birth cohort, and the Ji 2020 is -- so the -- I mean, they're measuring different things, so the -- you know, the Ji is looking at -- the 2020 is cord blood fetal blood, and the 2018 is as you mentioned.
Q. Right.
So, Dr. Hollander, they are different, right? They're different biomarkers?
A. They're different biomarkers.
Q. Yeah.
And in your rebuttal report, when you listed the biomarker studies, you only cited Ji 2020 and Baker, correct?
A. In my rebuttal in the section in biomarkers, yes, I included those two.
Q. And that's because the results of this don't fit your theory, right?
A. No, not necessarily.
Q. Okay. Let me know when you are

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ready to acknowledge that the outcome for ADHD and ASD are discordant when they studied maternal cord blood. Sorry, maternal plasma.
It might help you, Doctor, if you look at Table 2 on page 7 of 15.
Are you ready for a question, Doctor?
A. Could I have one more minute --
Q. Yeah.
A. -- to just put this into context and understand it?
Q. Because I don't want to get into a spat about time, but this is in his reliance materials.
A. Okay. Okay.
Q. Okay. Dr. Hollander, you reviewed this before today, right?
A. Yes, I have.
Q. Okay. And you chose not to include it in your rebuttal report, right?
A. I wonder if I -- I mean, I've seen this and thought about the issues. Let me just make sure that I haven't cited it at all in my rebuttal, so...
MR. DOVEL: If you're worried

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about time, why ask that question? You know whether it's in his rebuttal or not.
You want him to spend time looking through it?
MR. MURDICA: I think he should know what's in his reports and not, so I got to ask the question.
MR. DOVEL: Okay.
THE WITNESS: Okay. Well, so --
QUESTIONS BY MR. MURDICA:
Q. Okay. So you've reviewed it. You reviewed it before today, right, Dr. Hollander?
A. I have seen it before, and I've done a quick review of it now.
Q. And you'll take -- well, I will represent to you that it's not in your report or your rebuttal report or your amended report. So at some point if that's true, you decided that you didn't need to cite it, right?
A. Right. I don't think it is informative with regards to -- so, I mean,

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the two points I would make. One is, there was no effect in the ASD.
The second is, this is suggesting that there's some kind of a maternal factor associated with usage, right? Because it's occurring in maternal blood postpartum.
So it gets back to the same issue there as to whether or not, you know, there's some kind of a maternal or genetic or familial factor that influences the usage that relates to the outcome.
Q. Okay. Dr. Hollander, one of the reasons you just said you didn't include it is because there's no significant finding as to ASD, correct?
A. Well, there is no finding with regards to ASD. I see that.
I see that there are some findings as it relates to different models in terms of acetaminophen burden.
Q. If you look at Table 2, Doctor, there's nothing significant under any model with respect to ASD or other DD, right?
A. On that table, yeah.

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Q. Those are the outcomes, right?
This is -- it's titled "The association between maternal acetaminophen metabolites and the risk of ADHD diagnosis, ASD diagnosis or other developmental delay diagnosis in offspring."
Right?
A. But the -- I mean, the issue here is a particular plasma biomarker that's measured a few days after delivery.
Q. Okay. So to you, to Dr. Hollander, this biomarker study is not informative on whether acetaminophen causes autism and ADHD in offspring, correct?
A. Well, it's addressing whether or not there's a particular familial or genetic confounder that could be a factor in terms of understanding the relationship between APAP and ADHD.
Q. Dr. Hollander, do you know why there were discordant findings between ADHD and ASD?
MR. DOVEL: Objection. Form.
THE WITNESS: Well, let's see if the authors address that.

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QUESTIONS BY MR. MURDICA:
Q. Without having to go back and read it, you don't know sitting here right now --
A. I don't recall it off -- I mean, you're asking me to comment on the findings of this article.
Q. Right.
A. So I'd be able to comment on the findings of the article, but I need to be able to read it.
Q. Right.
It was on your review material -- your materials reviewed before you rendered your opinions here, correct, Doctor?
A. It is listed in the materials considered.
Q. Okay. For Ji 2020, Doctor, you know that the cord -- the biomarker was cord blood, right?
A. That's correct.
Q. And the cord blood was reflecting what was in the cord blood burden as of birth, right? The time of birth?

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A. It reflects fetal blood supply at the time of birth.
Q. Right.
And that was one snapshot in time at the time of birth, correct?
A. It's one -- yes, it's collected at one time period. It's not collected throughout the pregnancy.
Q. Right.
And that one day, the couple hours before birth, is not the only window where the fetus is susceptible to influenced-cause ASD and ADHD, correct?
A. Well, that -- that's correct.
Q. Okay.
A. I mean, the fetus would be susceptible to exposure before that one-day window.
Q. And the only measure in Ji 2020 is that one-day window at birth, correct?
A. That's -- that's one measure, right.
Q. Okay. And in your report, you're not critical of that one measure as a biomarker. In fact, you think it's very

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important, that one measure at the time of birth, correct?
A. Well, it does show a dose-response relationship as it relates to acetaminophen exposure during pregnancy.
Q. Okay. And Ji 2018 --
A. Yeah.
Q. -- you've disregarded because it's one snapshot of exposure in the peripartum period, correct?
A. Yeah. Well, it's not an exposure during pregnancy.
MR. MURDICA: Okay. I'd like to take a break so that I can save my last 15 minutes and figure out exactly what we're going to do with it. Just need five minutes.
Thank you, Doctor. I'll be right back.
THE WITNESS: Okay.
VIDEOGRAPHER: The time right now is 5:59 p.m., and we're off the record.
(Off the record at 5:59 p.m.)
VIDEOGRAPHER: The time right

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now is 6:07 p.m. We're back on the record.
QUESTIONS BY MR. MURDICA:
Q. Dr. Hollander, are you ready to proceed?
A. Yes, I am.
Q. Okay. You mentioned earlier about conducting animal studies.
Do you remember that testimony?
A. I mentioned animal studies. I'm not sure what you're referring to --
Q. Dr. Hollander -- oh, sorry.
I thought that you said that you've conducted animal studies before.
A. I have, yeah.
Q. All right. Not on acetaminophen, right?
A. No.
Q. But you've conducted animal studies and observed -- and observed behaviors in the rodents that you ascribe to different neurodevelopmental outcomes, right?
A. Yes. I mean, animal studies are important because they were a way for me to select compounds for therapeutic trials,

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actually. And if a compound can be effective in an animal model of autism, well, then that would be important to then give you support to consider a trial on humans.
Q. Dr. Hollander, tell us what the scent marking test is.
A. The scent marking test?
Q. Yes.
A. I'm not sure what you're referring to in terms of the scent marking test.
Q. Okay. Are you familiar with the rodent animal study for -- that's scent marking for neurodevelopmental outcomes?
A. I think I do in terms of sort of -- yeah.
Q. Okay.
A. It's not a -- that's not a standard model that I rely on in terms of sort preclinical testing for compounds for therapeutic trials.
Q. Dr. Hollander, in the scent marking test, would increase or decrease of scent be -- of scent marking be evidence of autism?

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A. I'm not familiar with that particular test. I could posit a guess, but I'm not sure.
Q. Okay. Are you familiar with the pup ultrasonic vocalization test?
A. Yes.
Q. Okay. And why don't you tell us how that test is conducted.
A. Well, that's a kind of test where you separate, I guess, a pup from the mother, and then the pup protests with ultrasonic vocalizations.
Q. Okay. And would -- Dr. Hollander, would an increase or a decrease in vocalization be evidence of autism?
A. I guess a decrease in the vocalizations would be associated with an impairment in the social domain.
Q. Okay. So your answer to that is decrease in vocalization?
A. Yes. If there's an impairment in vocalizations when you separate the pup from the mother, that would suggest social deficits which would be associated with

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autism model. So it looks at a particular symptom domain within -- relevant to autism.
Q. Okay. And, Dr. Hollander, are you familiar with the whole board explanation test? Exploration test?
A. Well, I'm familiar with things like the open field exploration test.
Q. Okay. How about the marble burying test? Are you familiar with that?
A. That, I'm familiar with.
Q. Okay. In your rebuttal report at page 35, you are talking about the Carey study.
Do you see that on page 35?
A. Ji claimed the Carey study was not addressed, is that what you're referring to?
Q. Yeah, that's part of it. Yep. In there.
A. Okay.
Q. And you -- and you cite it?
A. Yeah.
Q. You're relying on Carey for the hypothesis that oxidative stress is a biomarker for ASD outcome, right?

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A. Well, I mean, as discussed, it's a mechanism study, right.
Q. Right.
A. And it doesn't go all the way from mechanism to disorder, but it's a step in the link.
Q. And is it -- is it your testimony that Carey supported the link in the mechanism?
A. It supports the link, and the issue is, well, if you adjust for confounders, well, the strength of the association decreases based on the sample size, but the odds ratio is still above 2. So there's still a strong relative risk, but that because of the sample size, it doesn't reach statistical significance.
Q. Okay. And is that the best evidence you have, Doctor?
MR. DOVEL: Objection. Form.
QUESTIONS BY MR. MURDICA:
Q. Of your mechanism -- of your oxidative stress mechanism?
A. That's one piece of evidence in support of that.

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Q. It's the only piece of evidence you have in a human being, correct?
MR. DOVEL: Objection. Form.
THE WITNESS: Well, it's a -- it's a piece of evidence in human beings that shows a strong relative risk between oxidized glutathione and ASD, that it is a study that's underpowered. And so when you start to adjust for some confounders, the relative risk persists, but the statistical significance goes away.
(Hollander Exhibit 62 marked for identification.)
QUESTIONS BY MR. MURDICA:
Q. Okay. Let's see if that's true. We're going to mark this as Exhibit 62.
A. Well, and I guess maybe just to contradict also what you said, it's not the -- it's not the only evidence, and so I also cite the Anand study as well.
Q. Got it right here, Doctor.
A. Okay.
Q. That's next.

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A. Excellent.
Q. If we have time.
If you could please look at what's been marked as Exhibit 62, you have in front of you the Carey study, correct?
A. Yes.
Q. 2022. That's what you cited in your rebuttal report, right?
A. Yes.
Q. I'd like you to turn to the conclusions and just read the first sentence.
You recognize Carey's conclusion, do you not, Dr. Hollander, that overall they did not observe strong associations between maternal markers of oxidative stress in the late second and third trimester and ASD-related traits, right?
A. That's what the sentence says.
Q. Okay. And the second and third trimesters are -- that's your key window that you just testified to, right?
A. That is an important window.
Q. Okay. So you just said you think it's strong, and the authors said they did not observe a strong association.

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So that you disagree with the conclusion of Exhibit 62, correct?
A. Well, I mean, again, as a -- as an elevated odds ratio, it's -- when adjusting for different confounders and because of the sample size, you lose the statistical significance.
Q. All right. In any event, Doctor, you're relying on --
A. And by the way, also, just to continue with that thought, really.
So what they are observing is these -- this relationship between the traits and this measure of oxidative stress. So that's very interesting also.
Q. Okay. That's interesting. But at the end of the day, the conclusion of Carey does not support that there's a strong association between oxidative stress and the outcome of autism spectrum disorder, correct?
MR. DOVEL: Objection. Form.
THE WITNESS: Well, there is -- there is -- they're saying that this is suggestive evidence and that further work should be conducted.

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QUESTIONS BY MR. MURDICA:
Q. Okay. And the other study that you mentioned is Anand, right, Doctor?
A. That's right.
Q. Is that one any better for you, do you think?
A. I'm happy to review that with you.
Q. Okay. I just -- before you review it with me and I show you that it's not, I want to know your opinion as to whether that's helpful to your opinions. Anand.
MR. DOVEL: Objection. Form.
THE WITNESS: Well, I mean, it does suggest that higher concentrations are associated with ADHD diagnosis at an odds ratio of 2.1, is a marker of oxidative stress in cord plasma was associated with a higher odds of ADHD.
QUESTIONS BY MR. MURDICA:
Q. Okay. That's what you believe it concludes, right?
A. That's an interpretation of the

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results, yes.
Q. Okay. Did you come -- Dr. Hollander, did you come up with Carey and Anand on your own?
MR. DOVEL: Just a second.
MR. MURDICA: He can answer that. If he didn't, I won't ask him if it came from counsel. I just need to know if he came up with it on his own.
MR. DOVEL: Well, the way it's phrased, the Southern District of New York counts that as asking, so you're going to have to rephrase it.
QUESTIONS BY MR. MURDICA:
Q. Dr. Hollander, did you find the Anand article?
A. Did I find the Anand article?
Q. Yes.
A. Yes, it popped up in my search, and I also discussed it with other experts such as Dr. Cabrera.
Q. Okay. And did you find the Carey article?
A. Yes.

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Q. Okay.
A. And I also discussed that with Dr. Cabrera.
Q. On the oxidative stress point, did you find any other articles involving human beings and acetaminophen?
A. I guess I can -- to answer that, I could go to my --
Q. Do you recall, sitting here today, Dr. Hollander, finding any articles other than the Anand and the Cabrera -- Anand and Carey?
A. Well, I see that the Anand and the Carey are both mentioned in my rebuttal, and I could also look at my amended expert initial report and see if I cite additional references.
Q. Okay. If you found anything else that you thought supported your opinion, it would be in the rebuttal or the initial report, correct, Doctor?
A. It would be -- it would be in there. It would also be a wealth of information in the Cabrera report and rebuttal as well.

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Q. Are you relying, Doctor, on -- are you relying on Dr. Cabrera for the biological -- the plausible biological mechanism aspect, or are you opining on that yourself?
A. I've had the opportunity to speak with him, and I've had the opportunity to read his report and his rebuttal. I agree with that.
I am relying on my own reading of the articles.
Q. Okay. So your biological mechanism opinions stand on their own, and you don't need Dr. Cabrera. You're not relying on Dr. Cabrera, correct?
A. Well, that's correct. I offer opinions with regards to plausible biological mechanism in my reports.
Q. Okay. And you don't know which of those -- which mechanism is the most plausible biologic mechanism according to Dr. Hollander?
A. According to Dr. Hollander?
Q. Yes.
A. Well, I think impact on the

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endocannabinoid system is a very important --
Q. Okay.
A. -- mechanism. I do think that oxidative stress is an important biological mechanism. I think epigenetics is a very important biological mechanism as well.
Q. And all three of those, you believe, are causative between acetaminophen exposure and the outcomes of ASD and autism, right?
A. Well, all of them are plausible biological mechanisms by which exposure to acetaminophen can cause ADHD or ASD and neurodevelopmental disorders.
(Hollander Exhibit 63 marked for identification.)
QUESTIONS BY MR. MURDICA:
Q. Perfect.
Okay. We'll mark this as Exhibit 63, please.
All right. This is the last thing I'm going to be asking you about, Doctor.
Dr. Hollander, you now have in front of you Exhibit 63. This is the Anand

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study that you cited in your rebuttal report, correct?
A. It's 2021. And 2021, it does appear to be that. Yep.
Q. Okay. I'm just going to direct -- in the interest of time, because we're almost out of time, I'm going to direct you to page 10 of 16 for my question, Doctor.
If you look at the second paragraph under Discussion, it says, "These findings are in opposition to our original hypothesis that lower levels of amino acids involved in the synthesis of glutathione may explain the association between cord acetaminophen and ADHD risk."
Did I read that correctly?
A. Well, you read the sentence, yes.
Q. Okay. And do you disagree with the sentence as it appears in the Anand article?
A. Well, they're saying that increasing cord methionine and glycine partially statistically mediated the association between cord acetaminophen levels

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greater than 50th percentile and childhood ADHD diagnosis.
Q. And my question was, do you disagree with the sentence as it appears in the Anand article, the one that I read?
A. Well, there are -- they are suggesting that they -- these findings are different than what they originally hypothesized.
Q. Okay. And do you disagree with their findings, that they're not consistent with what they hypothesized?
A. Well, they're finding something that's a little bit different than what they originally hypothesized.
Q. Okay. Dr. Hollander, I'm really trying to be done with this here. This is -- this is the last question I'm asking.
Do you disagree that they did not confirm their theory that oxidative stress was the hypothesis to explain the connection between cord acetaminophen and ADHD risk?
A. The -- one thing that's

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interesting is they're finding certain things that are mediators of the association.
Q. Are you able to answer my question?
A. Well, if you look at their conclusions, "the oxidative stress biomarker, 8-hydroxy-deoxyguanosine, were associated with increased odds of childhood ADHD, and further that these other measures were partial mediators of the association between higher levels of cord acetaminophen and childhood ADHD."
Q. Dr. Hollander, my question was --
A. "These results suggest that oxidative stress mechanisms should be further explored to understand the link between perinatal acetaminophen exposure and risk of childhood ADHD."
You know, it's not unusual that you have a particular hypothesis, that you have findings that you may modify or revise your hypothesis according to the results. So I find that appropriate.
Q. Dr. Hollander, did you

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accurately portray the results of Anand in your rebuttal report?
A. Well, they're -- I mean, they're saying here there's oxidative stress biomarker is associated with the increased odds of childhood ADHD and that -- yes, so I think that that's accurate.
MR. MURDICA: Okay. If that's what you think, that's fine. I have no further questions.
CROSS-EXAMINATION
QUESTIONS BY MR. DOVEL:
Q. Sir, just keep that same document out.
Defendants' counsel was asking you about a particular sentence in Anand. I'd like you to read yourself the very next two sentences.
A. Okay. Could you please direct me to the page and the --
Q. Page 10.
A. Okay.
Q. Last paragraph. Sentences 2 and 3.
A. The sentence that begins, "This

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may suggest that"?
Q. And the one right above it.
A. Okay.
Q. The "however" --
A. "However, elevated levels of methionine, serine, glycine and glutathione were significantly correlated with the oxidative stress biomarker 8-hydroxy-deoxyguanosine. This may suggest that potential disruption of the homeostasis of glutathione synthesis by acetaminophen is associated with increased oxidative stress."
Q. Is that conclusion consistent or inconsistent with your opinions?
A. Well, that's consistent with my opinions.
Q. Let's turn to Ji 2018, Exhibit 61.
A. Yes.
Q. I'd like you to look at -- let's start with Table 3. It's on page 8.
A. Okay.
Q. Do you see where it reports the odds ratios for ADHD and ASD?
A. Yes, I do.

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Q. In your view, are the effects reported here from acetaminophen burden on ADHD and ASD discordant or concordant?
A. You know, as I was mentioning, so there's an elevated odds ratio for a relationship between acetaminophen burden and ADHD that's, you know, elevated across a number of different models.
The sample size is 188 individuals, and the p-values are all statistically significant.
If you look at the same with regards to the ASD, you know, the -- so the overall rate is lower, and the -- so the sample size is a lot lower. So it's only 44 as compared to, you know, a higher percentage of the population and the bigger number for ADHD.
So the odds ratio is pretty similar, actually, across all of these different models, whether it's ADHD or ASD. But the p-values aren't statistically significant, but the -- but the reason is that the sample size is less than a quarter of the size.

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So the -- to some extent, they're all elevated odds ratio, whether it's in ASD or ADHD, so that's a concordance. But the sample size is smaller, so the statistical significance is not as strong.
Q. Dr. Baccarelli, in his rebuttal report, has a discussion of comparing Ji 2018 and Ji 2020 where he concludes, "The Ji 2018 study, if anything, supports my conclusions rather than refuting them."
Do you agree with that?
MR. MURDICA: Objection to form.
QUESTIONS BY MR. DOVEL:
Q. Let me rephrase it.
He says, "The Ji 2018 study, if anything, supports my conclusions rather than refuting them."
MR. MURDICA: Objection to form.
QUESTIONS BY MR. DOVEL:
Q. Let me ask my question.
Do you agree or disagree with that statement?
MR. MURDICA: Objection to

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form.
THE WITNESS: I agree with that statement.
QUESTIONS BY MR. DOVEL:
Q. I'd like you to look at Exhibit 55. That's the Masarwa 2018 study.
You were asked some questions about the adjustment in Masarwa for parental diagnosis of ASD or ADHD.
Is adjusting for parental diagnosis something that would have an effect on showing the true association?
MR. MURDICA: Objection. Form.
THE WITNESS: Well, again, it's the same issue in terms of sort of genetic confounders. So if those genetic confounders affect the mechanism by which APAP exerts its effect or moderates that effect, then it would give you a false information with regards to the true association.
QUESTIONS BY MR. DOVEL:
Q. In your view, does Masarwa 2018, which does not make that adjustment, provide a better estimate of the effects of

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acetaminophen as compared to the adjustment that's done in Masarwa 2020?
MR. MURDICA: Object to form.
THE WITNESS: Well, I mean, the answer is yes. I mean, if there are genetic or familial factors that again mediate or moderate the effect, then if you adjust for those factors, then it interferes with what the true association is.
QUESTIONS BY MR. DOVEL:
Q. Let's look at Exhibit 58, the supplementary material for Alemany.
I want you to turn to page 5. We're going to talk about the description of the DNBC cohort in the second paragraph.
Do you have that in front of you?
A. Yes, I do.
Q. The second sentence there says, "At the first contact, women filled out a form that included questions regarding any supplement in medication use covering the period from four weeks before pregnancy to the gestational of reporting."

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Does that sentence indicate that there was no information taken about when the medication was taken?
MR. MURDICA: Objection to form.
THE WITNESS: Well, so I see that there are different contacts, and this is talking about the first contact, what's covering the period where they're asking.
But then there are other contacts, I guess, at 12 and 30 weeks, right?
QUESTIONS BY MR. DOVEL:
Q. Yeah, so I'm starting with the first contact.
A. Okay.
Q. Is it consistent with that sentence that the mothers would have given a report about the period from four weeks before pregnancy as well as a report about pregnancy?
A. Well, it doesn't -- you know, it doesn't specify in that sentence whether -- so they're asking for that, but

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they don't say whether or not they're asking about -- so they may be asking about it during that time period, but they may be recording it during -- for pregnancy or not during pregnancy.
Q. If we look at the last sentence -- rather the last two sentences, does that indicate that in classifying mothers as users of acetaminophen during pregnancy, that it included use before pregnancy?
MR. MURDICA: Objection to form.
THE WITNESS: No, it doesn't. And so that's what I meant, is that this sentence is not in accord with the earlier sentence. So the -- it's suggesting that when they classify the users, they're classifying the users based on whether or not they took acetaminophen during pregnancy or not.
But they're not classifying the users -- they may have asked about that, but they may not have classified

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them as using it during pregnancy.
QUESTIONS BY MR. DOVEL:
Q. If there were a study that had included in its analysis maternal use before pregnancy and had that -- and had lumped that in with use during pregnancy, so that a use of acetaminophen that would not cause autism or ADHD was lumped in, would that then bias the results towards the null?
MR. MURDICA: Objection to form.
THE WITNESS: Yes, it would.
MR. DOVEL: No further questions.
REDIRECT EXAMINATION
QUESTIONS BY MR. MURDICA:
Q. Okay. Staying on this exhibit.
Dr. Hollander, your interpretation of what the DNBC cohort counted as acetaminophen exposure is based on the -- not based on what was collected in the -- in the second line, but based on the last line: Mothers were classified as users of acetaminophen during pregnancy if they had taken any dose of acetaminophen at any time

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up during pregnancy.
Right?
A. Well, it's consistent with that, but it's also consistent with the idea that -- so what -- it is consistent with that sentence.
The earlier sentence doesn't -- so all it says is that they fill out a form. The form includes questions. The -- but it doesn't say how -- what exactly is on the form or how the form is specified, whether it asked questions about pregnancy use or use four weeks before the pregnancy.
Q. Dr. Hollander, you know that this is the cohort published in the Liew studies, right?
A. Yes.
Q. You could -- you could have gone -- before you just gave the answers to your counsel that are wrong, you could have gone, and should have gone as the expert here, to the Liew studies and figured out the correct answer, right?
A. There's nothing in the Liew study that suggests -- and in fact, didn't we

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do that? I thought that we were looking at the methods of the Liew study.
Q. I have time limited to the time your counsel used, so --
A. Okay.
Q. -- I am not asking you to go look now.
A. Okay.
Q. You know you could have gone to look at how Liew collected data for DNBC, correct?
A. That's right. And in the methods, it didn't specify what you're alleging.
Q. Okay. And you just, in response to a question your counsel asked you, said essentially that you disagree with Masarwa's 2020 analysis of their own study, right?
MR. DOVEL: Objection. Form.
THE WITNESS: No.
QUESTIONS BY MR. MURDICA:
Q. Okay. Didn't you say that Masarwa's interpretation of bias in its 2020 study is incorrect? It's not how you would

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interpret the bias, right?
A. Well, let's take a look at that again.
Q. You didn't look at it when your counsel was asking you questions, right, Doctor?
A. Well, I'm looking at it in response to your question.
Q. Okay. And, Doctor, just for the record, I want it to reflect that you were able to answer the question just fine when your counsel asked it, incorrectly, and now you're taking time to look at the study.
MR. DOVEL: Well, as long as we're making a record, it was a very different question that I asked him that you asked on a different subject altogether.
QUESTIONS BY MR. MURDICA:
Q. Dr. Hollander?
A. Yes.
Q. You disagree with the conclusions the authors of Masarwa 2020 drew from their bias analysis, correct?
A. That's correct.

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Q. Okay. Back to DNBC cohort.
Plaintiffs' counsel asked you a question about if prepregnancy exposures were included. You testified that it would bias the data to the null, and I think I interpreted that as meaning Dr. Hollander says it would make the association with acetaminophen in the outcome study look smaller.
Was that your testimony?
A. That misclassification would bias to the null.
But also in examining the methods of the manuscript itself doesn't mention anything about that. And in examining the supplement material that you just showed me, it's clearly inconsistent internally, and that the sentence, "Mothers were classified as users of acetaminophen during pregnancy if they had taken any dose of acetaminophen at any time up during pregnancy."
And that the earlier sentence that seems to be contradictory to that is actually -- it doesn't specifically specify.

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It's just telling you that they're asking about that time period, but it's not telling you that they're classifying that during that time period.
Q. Dr. Hollander, forget about the DNBC then.
You already agreed earlier, four of them plainly say they counted exposures 30 days during pregnancy, right? For the cohorts. You already agreed to that.
A. Well, they are saying -- maybe we should take a look at those sentences again, just to be clear.
Q. Go ahead, Doctor.
A. Okay.
Q. Okay. Some of the cohorts definitely counted exposures to acetaminophen for the 30 days before pregnancy, correct?
A. Well, it -- in reading that, there is -- there is a sentence that says that.
Q. Okay. Assuming that the cohorts do count exposure the month before pregnancy, here's my question for you.
Based on your experience that

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you talked about earlier, counseling your patients about medication during pregnancy, do you think that pregnant women have any concern about using pregnant -- medicine during pregnancy more so than they did before they're pregnant?
A. Could you rephrase that?
Q. Sure.
A. I'm not sure I understand that.
Q. When -- wouldn't a woman be more likely to take a medication before she knows she's pregnant than after she knows she's pregnant?
A. I mean, it depends on the symptom.
Q. Don't --
A. And it also depends on the risk versus benefit or the knowledge.
Q. You don't think women express more concern about taking medication once they know they're pregnant?
A. I think it depends on what's -- what are the guidelines or the -- what people are told in terms of whether medicines are considered to be safe or not.

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Q. Okay. So according to Dr. Hollander, a woman, before she's pregnant and after she knows she's pregnant, looks at medication and putting medication into her body the exact same way, correct?
A. It also depends on the symptoms. So there are some women who get symptoms during pregnancy. They wouldn't have those symptoms beforehand.
So, well, yeah, they would be more likely to take the medicine during pregnancy than before if they're -- if they're having more symptoms during the pregnancy than before.
Q. Okay. Dr. Hollander, if there is prepregnancy data included here, the use is more likely -- use of acetaminophen is more likely than during pregnancy, correct?
MR. DOVEL: Objection. Form.
THE WITNESS: Yeah. I guess the issue again is whether or not the symptoms and when are -- when are the symptoms more likely so that women will be taking medicine to deal with the symptoms. And also, what are the

risks versus benefit understanding with regards to the particular medication.

QUESTIONS BY MR. MURDICA:

Q. Okay. And when we were talking about Ji 2018, you stand by your testimony that the peripartum exposure in the peripartum -- sorry. The peripartum biomarkers in the blood is irrelevant to the analysis, despite the answers you gave to plaintiffs' counsel, correct?

MR. DOVEL: Objection. Form.

THE WITNESS: Well, maybe you can read back to me the statement that you're asking me to consider whether or not I stand by it.

QUESTIONS BY MR. MURDICA:

Q. Okay. I'm not going to go find it, Dr. Hollander, but let me just ask it this way.

A. Yeah.

Q. Prior to plaintiffs' counsel asking you questions that you answered, did you want to change any of your testimony that you gave me before that?

A. I think -- I think I would, because I understand it a little bit better. Yes.

Q. Okay. So you want to -- Ji, which you reviewed before you rendered opinions here, right? 2018?

A. Ji that I reviewed a while ago and which you gave to me and I tried to interpret it relatively quickly, but I didn't really have time to evaluate it, yeah.

Now I would like to have a better understanding, now that I've been able to review the manuscript better.

Q. Well, we're out of time, so I guess you're going to have to get the better understanding after the deposition.

That was ten days ago when you rendered your rebuttal report, right?

A. I'm not exactly sure how many days.

Q. Does that sound about right? July 28th?

A. Sounds about right.

MR. MURDICA: Okay. I have no further questions.

THE WITNESS: Okay.

MR. DOVEL: This is the conclusion of our deposition.

THE WITNESS: Okay.

VIDEOGRAPHER: The time right now is 6:48 p.m. We are off the record.

(Deposition concluded at 6:48 p.m.)

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CERTIFICATE

I, CARRIE A. CAMPBELL, Registered Diplomate Reporter, Certified Realtime Reporter and Certified Shorthand Reporter, do hereby certify that prior to the commencement of the examination, Eric Hollander, M.D. DFAPA, FACNP, was duly sworn by me to testify to the truth, the whole truth and nothing but the truth.

I DO FURTHER CERTIFY that the foregoing is a verbatim transcript of the testimony as taken stenographically by and before me at the time, place and on the date hereinbefore set forth, to the best of my ability.

I DO FURTHER CERTIFY that I am neither a relative nor employee nor attorney nor counsel of any of the parties to this action, and that I am neither a relative nor employee of such attorney or counsel, and that I am not financially interested in the action.

_____

CARRIE A. CAMPBELL,
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Dated: August 10, 2023

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ACKNOWLEDGMENT OF DEPONENT

I, ________________________, do hereby certify that I have read the foregoing pages and that the same is a correct transcription of the answers given by me to the questions therein propounded, except for the corrections or changes in form or substance, if any, noted in the attached Errata Sheet.

____

Eric Hollander, M.D. DFAPA, FACNP DATE

Subscribed and sworn to before me this

________ day of ________________, 20 ______.

My commission expires: ________________

Notary Public

ERRATA

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WORD INDEX